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SURGERY

A Monthly Journal Devoted to the Art and Science of Surgery

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SURGERY

VOL. 28 NOVEMBER, 1950 NO. 5

Original Communications

ABDOMINAL ACTINOMYCOSIS

AN ANALYSIS OF 122 CASES

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ACTINOMYCOSIS may be defined as a chronic suppurative or granulomatous disease caused by a specific organism, *Actinomyces bovis,* characterized by the formation of multiple abscesses, draining sinuses, abundant granulation tissue, dense fibrous scar tissue, and by the appearance of tangled mycelial masses (sulfur granules) in the discharges of involved tissues. Three regions of the body in man most frequently are involved: the cervicofacial, in 60 per cent of the cases; the abdomen, in 20 per cent; and the thorax in about 20 per cent. While a number of therapeutic agents have been used for cervicofacial lesions with equally good results, the prognosis in cases of pulmonary and abdominal forms has been grave despite the use of a multitude of local and systemic therapeutic measures including major surgical procedures. With the advent of chemotherapy and, shortly thereafter, of the antibiotics, however, a new era has begun in the treatment for this painful, slow-progressing, and debilitating disease, and the prognosis has improved immeasurably.

Good reviewed all cases of pulmonary and abdominal actinomycosis observed at the Mayo Clinic prior to 1929. Except for occasional reports of cases and a study of penicillin in the treatment of all forms of actinomycosis by Nichols and Herrell, no further comprehensive review of cases of this disease at the clinic has been attempted. In the past 35 years 122 cases of actinomycosis, primarily involving the abdomen or gastrointestinal tract, have been diagnosed at the clinic and those cases form the basis of this study.

HISTORICAL ASPECTS

Actinomycosis in the cervicofacial form had been recognized early in the nineteenth century, first in cattle and then in man. Bollinger, in 1875, recognized the parasitic nature of the organisms in the yellow granules obtained from the pus of the lesions and gave it the name *Actinomyces bovis* (ray fungus).

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Israël then cultured the organism and demonstrated its bacteriologic characteristics, including its anaerobic growth. Bostroem obtained organisms which were similar except that they grew under aerobic conditions at room temperature, and he postulated the exogenous theory, that the causative organism occurred freely in nature and had its normal habitat on grasses and grains. This was the most widely accepted concept at the turn of the century and has been advanced in many medical texts until recently.

Wolff and Israël, however, postulated the endogenous theory, that the causative organism was a delicate, preferably anaerobic organism which grew only at body temperature and was not found outside the body of animals or man. Through the efforts of many investigators, including Wright, Lord, and Trevett, Naeslund, Emmons, Cope, Slack, and Rosebury, over the past 40 years, the endogenous theory originally advanced by Wolff and Israël has been substantiated.

BACTERIOLOGIC FACTORS

Waksman and Henrici, in 1943, clarified the classification and bacteriologic characteristics of actinomycetes. The term "actinomycosis" had in the past been applied to any disease resulting from infection from any member of the Actinomycetaceae family as well as to the disease produced by *A. bovis*. An aerobic actinomycete, almost identical morphologically, had been described by Bostroem and many other investigators. This organism, too, in rare instances, produced a disease somewhat similar to that of *A. bovis*. Naeslund, Lord, and many other workers had identified aerobic actinomycetes from the oral cavity and sputum in addition to the anaerobic organisms of *A. bovis*. Requirements for oxygen as well as fragmentation of mycelia were used as bases of subdivision by Waksman and Henrici for their classification of pathogenic Actinomycetaceae into the genus actinomyces, which includes the micro-aerophilic and anaerobic pathogens and produces the disease actinomycosis. They placed the aerobic pathogens in the genus nocardia, which produces the disease nocardiosis.

While the organisms are similar in the majority of their morphologic characteristics, they are distinctly different in their cultural characteristics, and, while both produce granulomatous lesions, they are different in their mode of spread and habitat, and they respond to different therapeutic agents.

A. bovis is micro-aerophilic or anaerobic and nonacid-fast; in most instances it produces clumps or "sulfur granules" in the infectious process. It is sensitive to penicillin. It spreads mainly by direct invasion, and hematogenous spread is uncommon.

Nocardia asteroides is aerobic, partially acid-fast, occurs commonly in nature, tends not to occur in clumps or granules, is sensitive to sulfonamides, and commonly spreads via the blood.

INCIDENCE

Ruhräh, Cope, and Sanford and Voelker individually demonstrated that actinomycosis occurs throughout the world. The residence, occupation, yearly

incidence, and the age of each of the 122 patients constituting our series are shown in Figs. 1 and 2. The average number of cases each year at the clinic over the past 34 years was 3.6. There were 80 males and 42 females in the series. (Cervicofacial actinomycosis occurs in the ratio of 4 males to 1 female.) The preponderance of cases occurred in the adolescent and middle-aged groups, 102 of the 122 cases being of patients between the ages of 10 and 50 years. Forty per cent of the patients were farmers, 25 per cent were housewives, and 12 per cent were students, but many trades and professions were represented. Fifty-three patients lived in rural homes and 69 were urban dwellers.

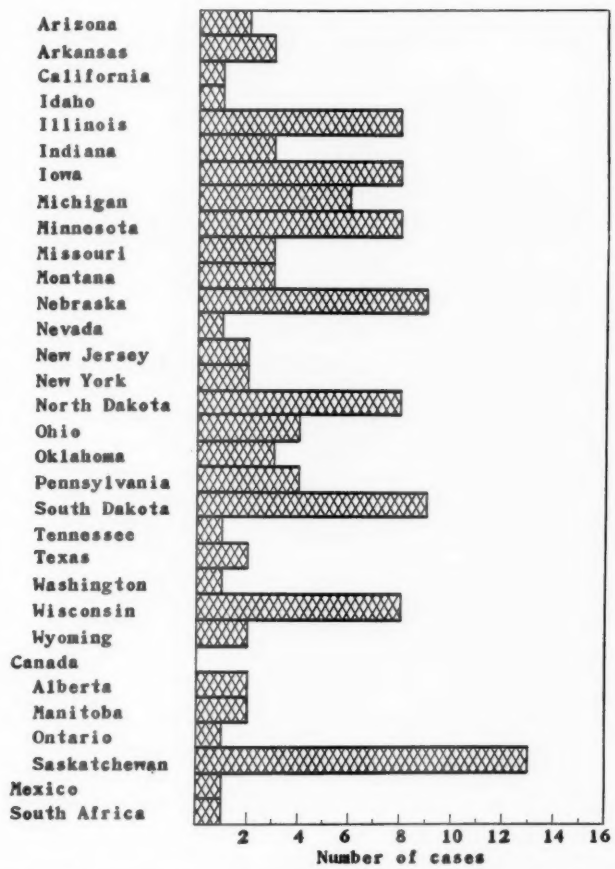

Fig. 1.—Geographical distribution of the 122 patients with abdominal actinomycosis.

PATHOGENESIS

A. bovis is a frequent inhabitant, leading a saprophytic existence, in the oral cavity,[37, 44, 46, 53] the respiratory tract[33] and the gastrointestinal tract[10, 13, 17] and especially in the former 2 locales in the presence of chronic, nonspecific infection.

The usual strains of these organisms appear to be of low virulence and they are unable to penetrate the barrier of an intact, normal mucous membrane. The peritoneum likewise offers resistance. The organism typically produces its

granulomatous lesions in connective tissue and muscles and rarely involves the mucosa or serosal linings primarily. In the cervicofacial form it has been established that either trauma or diseased mucous membranes from dental infections produce preliminary destruction of this normal mucosal barrier and allow actinomycetes to escape into the soft tissues of the neck and produce actinomycotic infection. Grotting, in a study of a large series (264 patients) with cervicofacial actinomycosis, found that in 46 per cent of the cases the disease occurred after dental extractions alone, and many of the remaining lesions were associated with dental caries or pyorrhea.

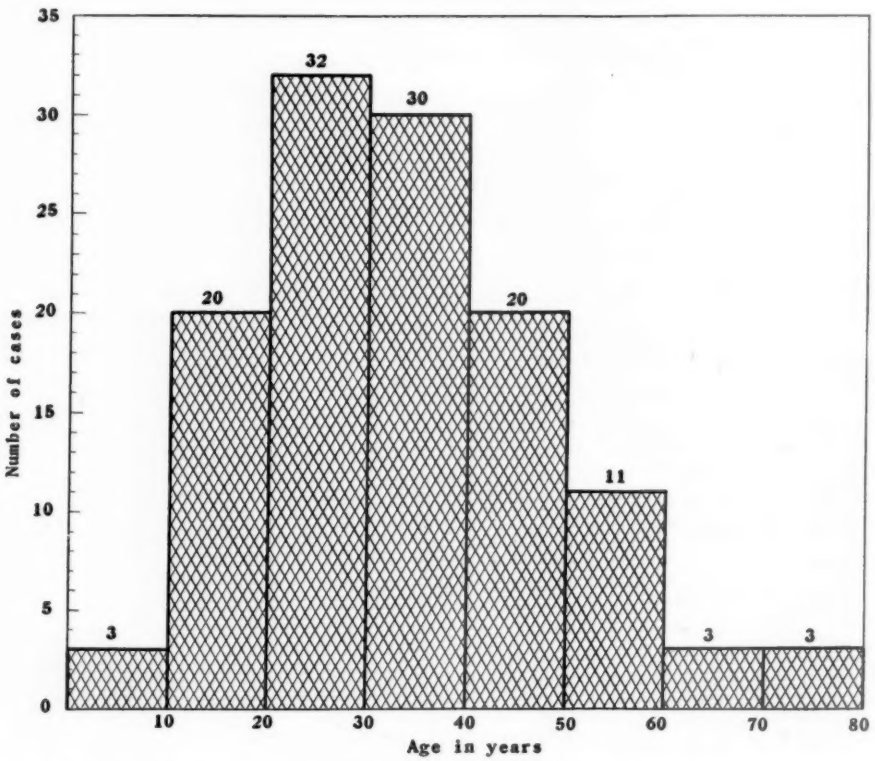

Fig. 2.—Age in decades of the 122 patients with abdominal actinomycosis.

In the abdominal form, the pathogenicity has not been so clearly defined. Evidence supports the idea that *A. bovis* occurs as 1 of the many organisms in the gastrointestinal flora. Three opinions given in the literature are: (1) that the organisms themselves are able to produce mucosal lesions primarily with ultimate extension to the other tissues; (2) that the organisms can penetrate the normal intact mucous membrane and produce the infection, and (3) that, as in the oral cavity, only when the normal barrier of an intact gastrointestinal mucosa has been destroyed by a disease process or by trauma can the organism penetrate into adjacent tissue and become pathogenic. Much clinical data support this last belief. In the vast majority of reported cases of abdominal actinomycosis, the infection has become evident several weeks or even months

after an acute, perforative, gastrointestinal disease such as acute appendicitis, perforating colonic diverticulum, perforated peptic ulcer, acute ulcerative disease of the intestinal tract, or after trauma. This was demonstrated well in our series of cases. Fig. 3 lists the gastrointestinal diseases which preceded or initiated the actinomycotic infection in the 122 cases. Typical acute appendicitis, usually of the perforative type, preceded the onset of the actinomycotic infection in 88 of our 122 cases (72.1 per cent). There were 3 undoubted and 1 probable case of acute perforated peptic ulcer with subsequent subdiaphragmatic actinomycotic abscesses. In a fifth case (Fig. 4), actinomycotic infection occurred after perforation of the gastric wall by 2 spicules of chicken bone. Spontaneous rupture of an actinomycotic abscessed spleen occurred months or several years later and emergency operation for this catastrophe revealed the spicules of bone lying in the gastrosplenic ligament.

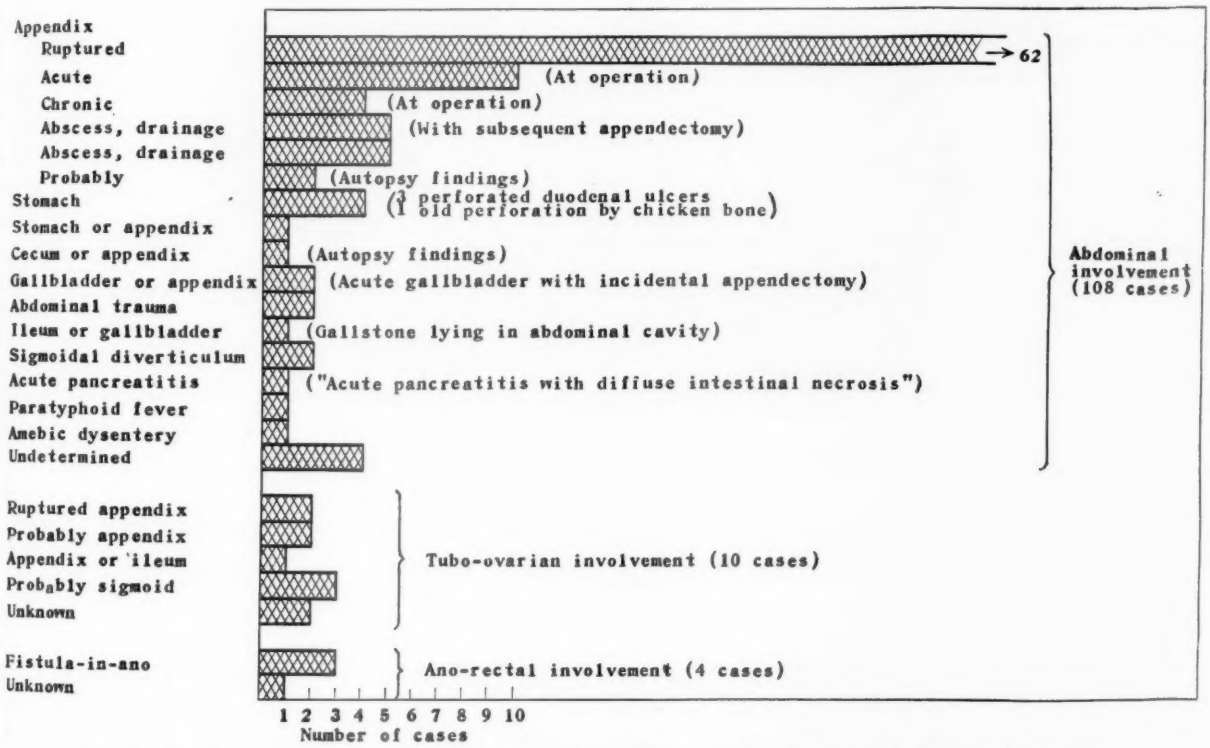

Fig. 3.—Sites of acute gastrointestinal perforative lesions or diseases which preceded the onset of actinomycotic lesions.

In 5 cases infection followed previous attacks of diverticulitis of the colon. In 3 of 4 anorectal cases, the patients had long-standing histories of fistula-in-ano. Abdominal trauma with the clinical impression of probable contusion or perforation of the bowel occurred several weeks prior to the onset of the infection in 2 cases. Acute cholecystitis in 1 case and a perforated gall bladder in another preceded infection, but incidental appendectomy had been performed in both cases at the time of operation and thus obscured the pathogenesis. Acute,

specific ulcerative infections of the bowel of various nature occurred in a few cases and their significance in the pathogenesis of the actinomycotic infection which followed weeks or months later can be based only on conjecture. Tubo-ovarian lesions occurred in 10 cases, and while ascending infection via the vagina has been recorded, the usual avenue is felt to be from gastrointestinal perforation, most frequently appendicitis. In only 3 of these 10 cases previous disease of the appendix or bowel could not be implicated in the pathogenesis. It is significant that in tubo-ovarian disease involvement of the right adnexal structures usually occurs first; extension to the left occurs later, implicating the appendix as the most frequent etiologic site. History of 2 primary acute gastrointestinal disorders was not present in only 7 of the 122 cases.

Fig. 4.—Multiple actinomycotic abscesses can be seen in the spleen, which ruptured spontaneously. Old clotted blood surrounded the spleen, which was cut in half. The patient, a man 44 years of age, was found to have 2 spicules of chicken bone lying in the thickened fibrotic gastrosplenic ligament. They had apparently perforated through the gastric wall some time previously, permitting actinomycetes to escape into adjacent tissues where they produced infection.

Bacteriologic proof that these preceding diseases were not primarily due to *A. bovis* could not be definitely established in this study as these episodes occurred elsewhere and the patients were usually referred to the clinic after onset of the actinomycotic process. In the great majority of these cases, however, the patient had typical acute appendicitis of short duration (12 to 24 hours), often with perforation and gangrene. *A. bovis* alone does not produce the pathologic picture presented by these patients. The age of each patient in these cases was that age at which acute nonspecific appendicitis occurs. Perforations elsewhere in the gastrointestinal tract were of nonactinomycotic origin, that is, typical perforated peptic ulcers, sigmoidal diverticulitis, and so forth.

Contamination of the abdominal cavity with contents of the bowel during surgical procedures may result in infection. In 6 cases in our series normal or

"chronic" appendices were removed, but actinomycosis developed soon after. Warwick stated, "It is quite conceivable that the appendectomy itself may have been the cause determining the onset of actinomycosis in a certain number of cases."

Many features in the pathogenesis remain obscure. Primary involvement of the gastrointestinal mucosa may occur, but the definite resistance of the mucous membrane to infection with *A. bovis* would seem to indicate that another mode of attack is more likely. When the frequency with which ulceration, abrasion, and superficial erosions of the intestinal mucosa must occur is considered, as well as the frequency with which appendicitis occurs, it is difficult to understand why abdominal actinomycosis is not commoner. Previous sensitization[41] and resistance of the host, virulence of the various strains, stasis of the fecal stream, and other unknown factors must play a role in production of the disease.

PATHOLOGIC ASPECTS

Grossly, the lesions of actinomycosis are characterized by the presence of firm indurated masses, which are poorly circumscribed, and by overlying skin of a brawny, dusky red. Over a period of days or more frequently weeks, the mass softens and cutaneous sinuses appear which tend to fibrose and heal and re-form elsewhere. Involved tissues are destroyed and replaced by abundant granulation tissue with multiple communicating abscesses and sinuses. Marked reaction occurs—1 area may be undergoing necrosis and an abscess may be forming while an adjacent area undergoes fibrosis. Drainage may be thin, yellowish, and serogangrenous or purulent, containing tiny yellow or brown "sulfur granules." On cut section the lesions reveal multiple abscesses of all sizes giving a honeycombed appearance with varying amounts of dense fibrous tissue.

The microscopic picture is one of micro-abscesses, granulomatous formation, suppuration and fibrosis (Figs. 5 to 9). The type of necrosis is liquefactive rather than caseative, with an abundance of leucocytes, occasional lymphocytes, monocytes, plasma cells, and histiocytes. Phagocytic giant cells containing lipoid material and lipoid histiocytes in part give the yellow appearance to the tumor. Actinomycetes frequently are not seen in sections of tissue, but when present occur as a colony or sulfur granule lying in the center of a micro-abscess "in a pool of pus." The central portion of this granule is most often composed of a dense network or mesh of fibrils, mycelial filaments, which stain well by Gram's method. Around the periphery of the colony, the ends of individual filaments project radially, and are enveloped usually by eosin-staining hyalin clubs which seem to form as the result of contact with the surrounding tissues. Clubs are not formed in laboratory mediums and occasionally are not seen in diseased tissues.

Surrounding each actinomycotic granule is a zone of liquefactive necrosis containing numerous polymorphonuclear cells, then a zone of histiocytes, then fibroblasts and collagenous fibers, and finally dense fibrous tissue. Mixed infection usually occurs in these lesions, and many contaminating bacteria are

seen. Streptococci, staphylococci, diphtheroids, escherichia, and other bacteria from the intestinal flora undoubtedly are factors in extension of the pathologic process.

Actinomycotic lesions arise in structures in contact with the site of ulceration or perforation of a viscus, or in pockets or recesses in which gastrointestinal

Fig. 5.

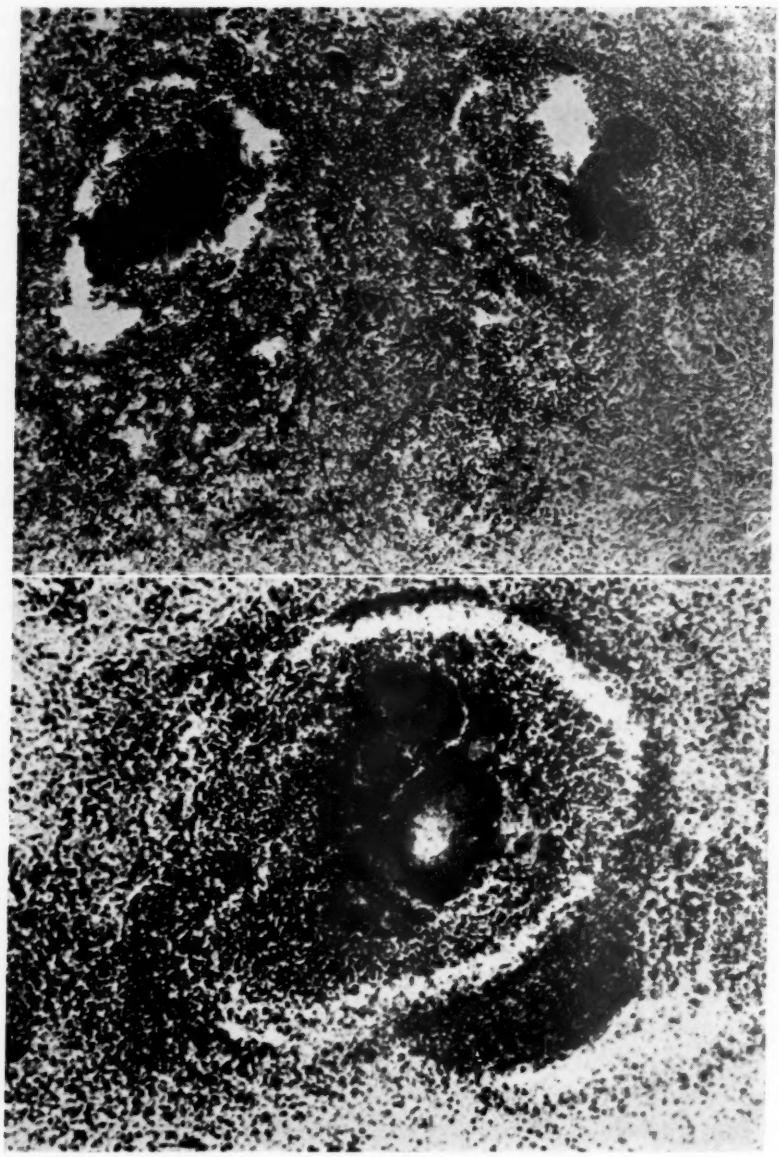

Fig. 6.

Fig. 5.—Two typical colonies of *A. bovis* are shown centered in micro-abscesses. Inflammatory tissue and then fibrous tissue surround the abscesses. The tissue is from the right iliac fossa of a white man 30 years of age (hematoxylin and eosin, ×85).

Fig. 6.—Colonies of *A. bovis* in a "pool of pus." Many polymorphonuclear leucocytes, and some lymphocytes, mononuclear cells, histiocytes, and fibroblasts are present in the surrounding tissue (hematoxylin and eosin, ×100).

contents have collected in the abdominal cavity. In most cases, involvement of the intestinal mucosa cannot be demonstrated, and even when the bowel is involved in the often huge inflammatory masses, the mucosa is seen to be intact. For this reason, "gastrointestinal," "ileocecal," and "appendical" actinomycosis are not accurate descriptive terms for the lesions of abdominal actinomy-

Fig. 7.

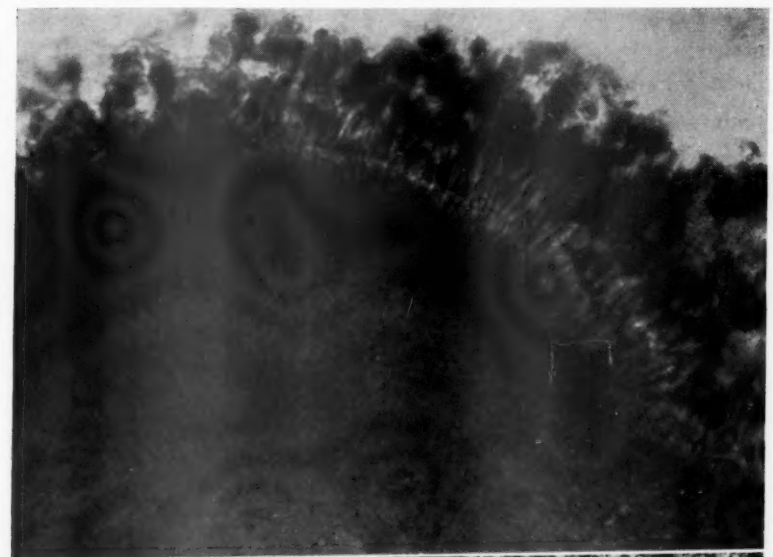

Fig 8.

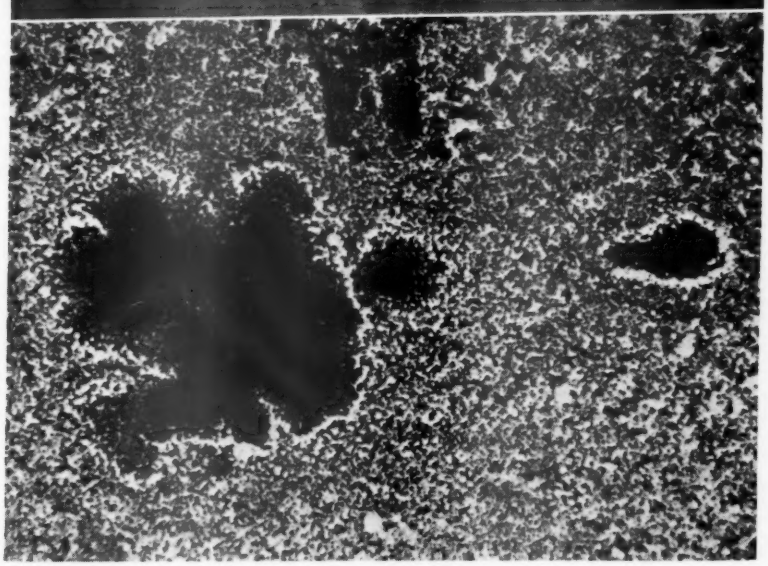

Fig. 7.—Portion of an actinomycotic colony under higher magnification. Radiating mycelia and "clubs" are well demonstrated at the periphery of the colony. It is this raylike appearance for which the organism was named "Actinomyces" (ray fungus) (hematoxylin and eosin, ×720).

Fig. 8.—One large colony and 2 small colonies of *A. bovis* in inflammatory and fibrous tissue from the abdominal wall. The patient was a white woman 45 years of age who had had a perforated appendix removed several weeks prior to the onset of the actinomycotic infection which involved the right ovary and the abdominal wall (right lower quadrant) (hematoxylin and eosin, ×70).

cosis. Typically the organisms penetrate into the retroperitoneal tissues and tissues of the abdominal wall, and there the initial actinomycotic lesion is found. Brockman urged dropping the terms "ileocecal" or "appendical" actinomycosis, and preferred the term "right iliac fossa actinomycosis," "because in actinomycosis the intestine and appendix are themselves usually free of the actual lesions, while the muscles and connective tissue of the right iliac fossa are the primary seat of the disease." Occasionally, as in tubo-ovarian actinomycosis or involvement of the anterior abdominal wall, the process is found to be well localized in these areas, and has left little or no trace of its source from the appendix or intestine. The location and areas of extension in the 122 cases comprising our series are given in Fig. 10. The tendency toward involvement of structures of the right side of the body is apparent and is to be expected considering that the appendix is the commonest site of perforative gastrointestinal disease in man. The right iliac fossa (right lower quadrant of the abdominal wall) was involved in 100 cases and the left in 31 cases, both sides being affected in some cases.

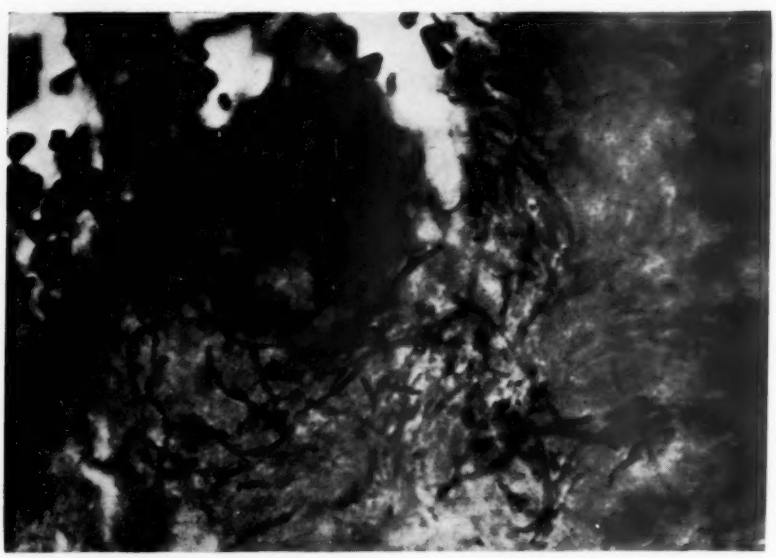

Fig. 9.—High magnification of the branching mycelial filaments in an actinomycotic colony demonstrating gram-positive reaction. The mycelia are sparsely distributed in this colony, but more frequently are dense. The tissue is from the right iliac fossa of a white woman 30 years of age. (Brown gram stain, ×1,200.)

Extension of the lesion is by direct continuity in most instances, and few structures are resistant to its attack. Spread is usually directed away from the bowel and peritoneal cavity, with wide extension through subperitoneal or subcutaneous connective tissue. Muscles are often infiltrated with resultant destruction and fibrosis. Bone is infrequently attacked, but occasional involvement of vertebral bodies is seen. The lymphatic system is only rarely involved and then fibrosis occurs; the lesion does not spread by way of the lymph channels. Hematogenous spread is uncommon, but rarely metastatic abscesses have been demon-

strated in distant organs. As Weed and Baggenstoss recently have shown, however, many of these metastatic "actinomycotic" abscesses in reality were produced by hematogenous spread of other contaminating organisms, and *A. bovis* could not be identified in them. In our series of cases involvement of liver, lungs, or kidneys was usually caused by direct extension of the infectious process from perinephritic, subdiaphragmatic, or subhepatic abscesses.

CLINICAL COURSE

In our series of 122 cases 103 patients had had emergency surgical procedures for acute inflammatory or perforative gastrointestinal lesions. It is important to realize that abdominal actinomycosis occurs as a complication of

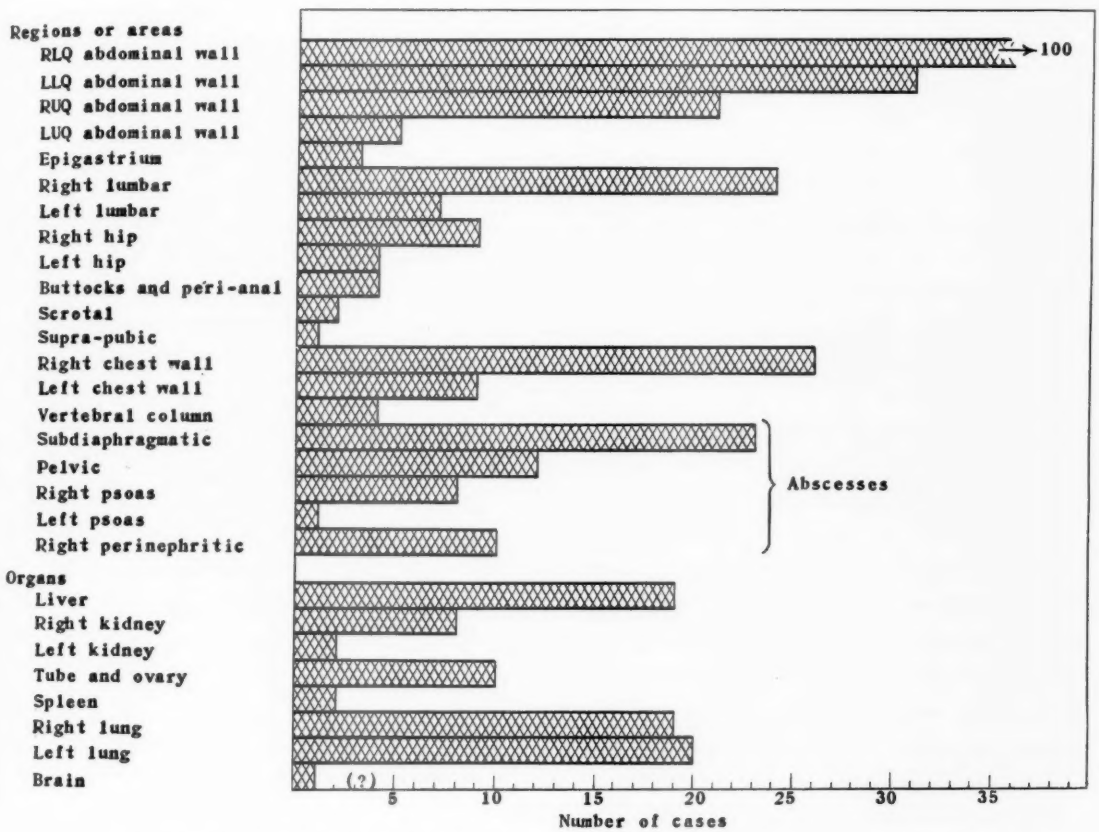

Fig. 10.—Regions of the body or organs involved by the actinomycotic infection.

other acute illness and probably seldom occurs as a primary disease of the gastrointestinal tract. Convalescence may have appeared normal and the operative wound to be healing satisfactorily, but a hard, fixed, nontender mass may form near the operative site or in the flank or pelvis. At times a persistent sinus in the operative wound may be the first indication of this complicating disease. The mass is firm and indurated, but, after days or weeks, softens, becomes tender and painful, and the overlying skin appears edematous and dull

red. With liquefactive necrosis of the mass, formation of an abscess occurs, and cutaneous sinuses form and drain a yellow or brown thin material which later becomes purulent. The sinuses tend to close leaving puckered scars, only to break down again or reform elsewhere, as extension progresses. The disease is characterized by its extreme chronicity, the sinuses having formed over a period of weeks or even months. The mass and sinuses may remain localized in the flank or abdominal wall for months or years. Usually, however, extension gradually occurs with involvement of muscular and fascial structures and results in painful contractures and deformities. Frequently the right hip becomes flexed because of involvement of the iliopsoas muscle.

Early in the course of the disease, systemic reaction may be minimal—perhaps only low-grade fever, slight weakness, and malaise. Extension may occur sporadically with episodes of acute systemic reaction, formation of abscesses and drainage through cutaneous sinuses, followed by periods of apparent recovery. With continued extension, loss of weight, anemia, and generalized debility become marked. The patient is pale, listless, and irritable and becomes bedridden. Dependent edema due to malnutrition and loss of porteins becomes evident. Death may occur by direct extension of the process to the liver, kidneys, or lungs, but the patient usually dies from pneumonia or some other acute infectious process. The many contaminating bacteria present in the lesions undoubtedly govern the rapidity with which the process develops and its ultimate outcome, as the granulomatous lesions produced by actinomyces characteristically tend to be chronic and localized and spread mainly by direct extension.

When the lesions remain localized, spontaneous cures may occasionally result, as occurred in several cases in our series in which the process was limited to a portion of the anterior abdominal wall. The anorectal lesions tend to remain localized to the perineum, scrotum, and buttocks. Tubo-ovarian lesions usually remain localized and an adnexal mass of unknown etiology may be the only finding prior to surgical exploration. Not infrequently, however, intermittent episodes of intestinal obstruction occur in these cases as the bowel becomes adherent to the inflammatory mass.

The course of the disease was definitely more rapid in the cases of actinomycosis after perforation by peptic ulcer—probably because extension from resulting subdiaphragmatic abscesses quickly involved liver and lungs by direct extension. This was true in subdiaphragmatic abscesses formed after appendical perforation, also.

In few other diseases does the sedimentation rate of erythrocytes show as marked acceleration as was shown in our series. Values ranging from 110 to 130 mm. per hour (Westergren) were present routinely in cases in which the disease was extensive, and the average sedimentation rate for all cases in which it was employed was 98 mm. per hour. Moderate leucocytosis usually is present, which may become marked during acute exacerbations of the disease. In our cases the average number of leucocytes was 13,200. Hypochromic anemia and marked depletion of proteins frequently occur.

DIAGNOSIS

Diagnosis can be established positively only by microscopic identification of the causative organism, *A. bovis,* and by culture of the organism. Demonstration that the mycelial filaments are gram-positive is essential for morphologic diagnosis. The most favorable specimens for obtaining these granules are the pus from newly opened abscesses, and the material obtained from curetting the walls of the sinus tracts. It should be stressed that the granules frequently are not found, and numerous attempts may be necessary before identification results. Large specimens of the material are necessary for both morphologic and cultural identification of the organisms. Other micro-organisms may form granules.

The importance of obtaining cultures of the organisms cannot be overemphasized, not only because of identification of the organism itself, but because the individual strain can then be tested as to sensitivity to various chemotherapeutic and antibiotic drugs, and is thus a great aid in instituting proper therapy. As Weed and Baggenstoss have demonstrated, strains of actinomyces can probably be bacteriologically distinguished from nocardia only by means of cultures.

It is true that cultures of the organism require special mediums, take 10 to 14 days and cannot always be obtained. However, continued effort may prove gratifying and repeated cultures always should be attempted.

Positive diagnosis, either microscopically or culturally, may be difficult. In 8 of our 122 cases the diagnosis was established only at necropsy, despite frequent attempts to identify the organisms. A tentative diagnosis, however, can be made on the basis of the patient's history and course of the disease, and proper therapy will greatly benefit the patient. The clinical response may aid in confirming the diagnosis made on clinical judgment.

All tumefactive lesions, whether inflammatory, benign or malignant, occurring in the abdomen, retroperitoneally, or in the abdominal wall, must be considered in the differential diagnosis. Appendical abscess, ovarian or renal tumors, subdiaphragmatic abscesses of any etiology, and malignant disease of the colon or stomach will occur more commonly than abdominal actinomycosis. Talc, lipoid, or other foreign-body granulomas may resemble abdominal actinomycosis. Any condition resulting in cutaneous sinuses and fistulas must be considered, and actinomycosis excluded. Nocardiosis rarely occurs primarily in the abdomen but produces widespread lesions throughout the body, and tends not to remain localized as does actinomycosis. Tuberculosis, blastomycosis, and other deep mycoses which produce granulomas must be differentiated.

Eight patients underwent operation with the clinical impression that an indeterminate mass present in the abdomen of each was probably malignant. The surgeon's impression at operation also was that of malignant disease, until biopsy of specimens revealed inflammation.

TREATMENT

The patient who has this chronic, debilitating disease not only must combat the effects of the specific organism, *A. bovis,* but also the toxic effects of numerous

contaminating bacteria as well. A high vitamin, high caloric, and high protein diet is essential. Measures must be instituted to combat anemia and diminished protein reserve if any other treatment is to be effective. Gage, Lyons, and DeCamp demonstrated the value of studies of blood volume in estimating the extent of these deficiencies. Multiple transfusions of whole blood are necessary in many instances to improve the operative risk and promote healing of wounds.

Numerous local and systemic medications have been used. Iodides and irradiation were used with encouraging results in cases of cervicofacial lesions, and in the localized abdominal form in conjunction with surgical procedures. Nevertheless cures in the abdominal or pulmonary types and in extensive cervicofacial lesions have been reported only occasionally, and these usually after months or years of treatment. Colebrook and Henrici and co-worker demonstrated that solutions of potassium iodide had no specific action on the organism

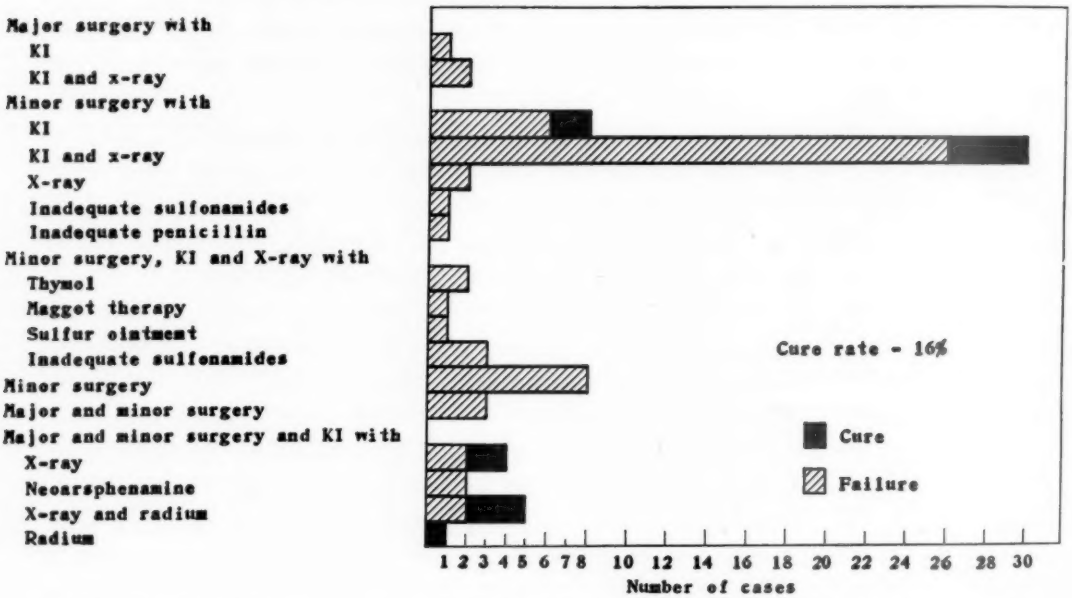

Fig. 11.—Results of therapy in 75 cases of abdominal actinomycosis in which neither penicillin nor sulfonamides were used.

itself, and that any beneficial action they may have is due to their effect on tissues rather than any bacteriostatic effect. The same is undoubtedly true of irradiation therapy. At the present time, the use of iodides or irradiation is probably outmoded.

Copper salts, vaccines, thymol, preparations of gold, arsenicals, crude extracts of lymph gland, and other preparations have been used with little effect and have been discarded. In our series, the rate of cure for all methods of treatment other than those of adequate sulfonamides or penicillin was 16 per cent (Fig. 11).

Sulfonamide compounds have been utilized in the treatment of actinomycosis since 1937. Sulfadiazine, or combinations of the sulfonamides which include sulfadiazine, seem to be the most effective of these chemotherapeutic drugs and

are recommended in generous dosages and in repeated courses over a period of months. Cutting and Gebhardt demonstrated that sulfonamides had an inhibitory effect on *A. bovis* in vitro. Keeney and co-workers demonstrated that while sulfonamides did inhibit the organism and had a lethal effect on it, yet the action required too high a concentration of the drug for the patient to maintain. As Dobson, Holman, and Cutting suggested, favorable results obtained with the use of sulfonamides may be those which exist in the combating of secondary invaders in the infection, thus allowing the natural bodily resistance to overcome the actinomyces. Whatever its action, sulfonamide greatly improved the prognosis in this condition. In our series, the rate of cure or improvement was 38.7 per cent (Fig. 12) in those cases in which sulfonamide therapy was used. Kolouch and Peltier reported a rate of cure of 56 per cent in those cases in which sulfonamides were used.

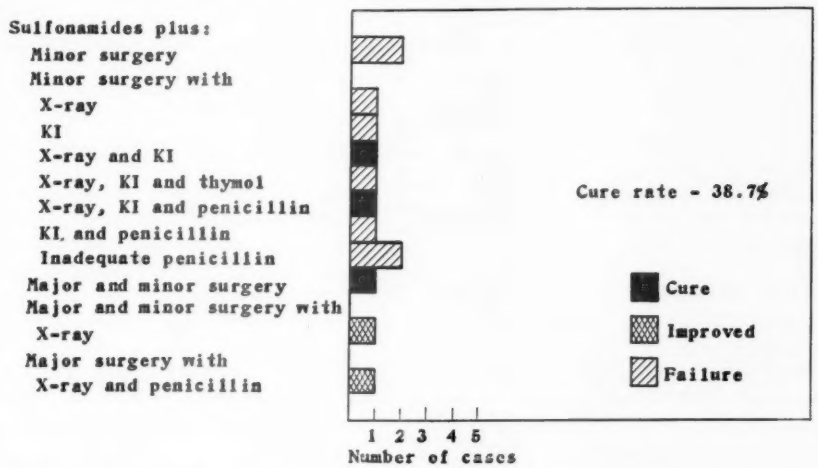

Fig. 12.—Results of therapy in 13 cases of abdominal actinomycosis receiving adequate sulfonamide therapy. The rate of cure or improvement was 38.7 per cent.

Lyons and associates demonstrated that aerobic actinomycetes (nocardia) were susceptible to sulfonamides with immediate clinical response on institution of the drug. Benbow and associates and Kirby and McNaught subsequently reported cures of nocardiosis with sulfonamides. Nocardiae are susceptible to sulfonamides in vivo and in vitro, and sulfadiazine remains the drug of choice in the treatment of nocardiosis. Drake demonstrated that penicillin is not effective in inhibiting nocardiae in vitro.

In 1941, British investigators[1] reported that the organism, *A. bovis,* was susceptible to penicillin in vitro. Subsequent investigations[2, 3, 29, 54] corroborated this finding. Keeney and co-authors reported that *A. bovis* was inhibited and apparently killed by a concentration of 0.01 Oxford unit of penicillin per cubic centimeter of medium, that the reaction of the organism to the drug was more like that of a bacterium than a fungus, and that, in their studies, penicillin was far more effective than the sulfonamides. Selbie and co-workers reported that in 10 strains of *A. bovis* obtained from infections of human beings, all were inhibited by therapeutic levels of penicillin. Boand and Novak recently

demonstrated that, in vitro, all strains of *A. bovis* which were tested developed little or no resistance to penicillin despite repeated transfers over a period of 3 months. At the clinic all strains cultured from actinomycotic patients have likewise been susceptible. Of 35 collected cases of abdominal actinomycosis reported in the literature[4, 8, 14, 15, 22-25, 30, 32, 36, 40, 43, 45, 49, 50, 52, 56] in which the patients were treated with penicillin, cure resulted in 23 cases and improvement in 8 cases. In only 4 cases was failure reported, a rate of cure or improvement of 88.9 per cent. Of the 24 cases in our series in which adequate penicillin therapy was used (Fig. 13), 15 patients were cured, and 8 were improved or probably cured but too recently to evaluate; only 1 failure occurred, and the rate of cure or improvement was 95.8 per cent. Our dosages of penicillin varied from 500,000 to 1,200,000 Oxford units daily for from 4 to 6 weeks. Frequently, repeated 2 week courses were utilized. Dosages of not less than 1,000,000 Oxford

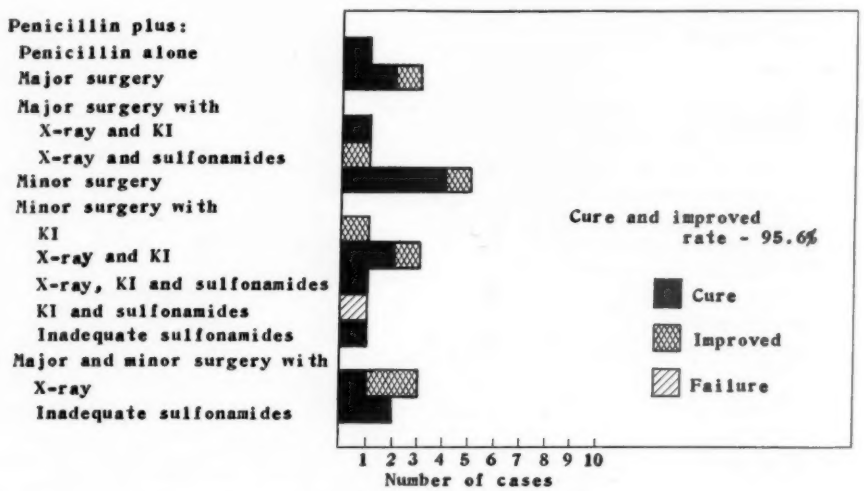

Fig. 13.—Results of therapy in 24 cases of abdominal actinomycosis receiving adequate penicillin therapy in addition to other forms of therapy.

units daily seem to be indicated. Total dosages varied from 10,000,000 to 50,000,000 Oxford units. Dosage of penicillin will vary with the particular strain of the organism, and its sensitivity to penicillin is best determined by in vitro tests of its susceptibility to the drug. The extent of involvement, the course of the disease, and the clinical response to the drug will aid in determining the proper dosage. Sanford and Barnes recently demonstrated that massive dosages of penicillin (10,000,000 to 20,000,000 Oxford units daily for a total of 500,000,000 Oxford units) may result in immediate response and cure, where the usual dosages of penicillin have not elicited response. Sulfadiazine was used in conjunction with penicillin in the majority of collected cases, and other clinicians have recommended that the 2 drugs be used together. In our series, penicillin alone was used in the majority of cases with excellent results. In the 1 case in which penicillin therapy failed, sulfadiazine had been used in conjunction with it.

Other antibiotic agents may prove to be of equal or even greater value than penicillin in the treatment of actinomycosis, but its low toxicity even in massive dosages and its effectiveness thus far in the cases treated indicate its present value. Meleney and associates demonstrated that bacitracin is effective against *A. bovis,* and its use may be indicated in the future. Streptomycin has been demonstrated to inhibit most strains of *A. bovis* in vitro, but Boand and Novak have shown that the organisms develop rapidly and retain a marked resistance to streptomycin. Neither bacitracin nor streptomycin was used in the cases in this series.

The role of surgical procedures in the treatment of actinomycosis continues to be of major importance. Because, in most instances, the patient is 1 on whom the surgeon has recently performed an emergency surgical procedure for an acute perforative gastrointestinal lesion, the care and treatment of this complication (actinomycosis) will be of particular concern. The concept that actinomycosis is as much a complication of acute perforative diseases of the bowel as is a subdiaphragmatic or pelvic abscess of any other bacterial etiology has not been properly emphasized. The surgical ideal in the past has been complete extirpation of all diseased tissue, but the extent of involvement in many abdominal cases made this ideal impossible. Brickner reported good results in pelvic actinomycosis using a bold persistent surgical attack. In 1936, Wangensteen stressed the importance of adequate surgical evacuation of abscesses with removal of all dead tissue, and the local use of zinc peroxide in the wounds.

With the advent of penicillin, an effective systemic therapeutic agent, surgical therapy has been mainly relegated to measures which will allow increased penetration of these agents into the involved tissues. When abscesses form, adequate drainage should be instituted. Incision and drainage of the abscesses relieve the severe pain and tenderness produced by their formation, lessen the possibility of extension of the process, and may aid in diagnosis as the sulfur granules are most frequently found in drainage after incision. Radical removal of diseased organs may be necessary, but probably this procedure should be postponed until recurrences occur after adequate trials of chemotherapeutic agents indicating that such a measure is necessary. In this series it was noted that recurrences occurred in the lesions with tubo-ovarian involvement despite large dosages of penicillin, and probably extirpation of these lesions is indicated wherever the optimal occasion for surgical excision presents itself. Surgical procedures were utilized in the treatment in each of the 108 cases in the series in which follow-up data were available. Radical procedures included splenectomy, nephrectomy, resection of tubo-ovarian abscesses, and resection of bowel. Minor surgical procedures included incision and drainage of abscesses, curettage of sinuses and fistulas, and excision of sinus tracts.

SUMMARY

A. bovis, the causative organism of abdominal actinomycosis, is found only in human beings and animals and leads a saprophytic existence in the flora of

the mouth, the respiratory tree, and the gastrointestinal tract. It appears to be incapable of penetrating an intact, normal, mucous membrane and becomes pathogenic only when this barrier has been destroyed by disease or trauma, and the actinomycetes have escaped into tissues which are less resistant to their growth. In most instances, therefore, abdominal actinomycosis probably occurs as a complication of an acute perforative or ulcerative disease of the gastrointestinal tract. Of the 122 cases of abdominal actinomycosis comprising our series, 103 patients had had emergency surgical procedures for acute gastrointestinal lesions prior to the onset of the actinomycosis. Typical acute appendicitis, usually perforative, preceded the onset of the infection in 88 patients; 4 patients had had perforations of peptic ulcer and 1 had had perforation of the gastric wall by a chicken bone. Sigmoidal diverticulitis, abdominal trauma, and other gastrointestinal ulcerative or perforative diseases accounted for other emergency procedures. In only 7 of the 122 cases there was no apparent history of such a previous acute illness.

Abdominal actinomycosis occurs most frequently in the young adult and middle-aged groups, has a widespread geographical distribution, affects people in all occupations, and affects males approximately twice as frequently as females. It is an uncommon, but by no means rare, disease. The pathologic aspects of the lesions have been described, and extension proceeds usually by direct invasion of adjacent tissues. Microscopic identification and culture of the organism are essential in diagnosis of the disease.

Treatment of abdominal actinomycosis consists of strenuous dietary and supportive therapy, including multiple transfusions of whole blood as indicated. The drug of choice is penicillin in dosages of approximately 1,000,000 Oxford units daily for from 4 to 8 weeks. The duration of treatment and the optimal dosage will vary depending on the response of the patient to treatment and the susceptibility of the individual strain of *A. bovis* as demonstrated by culture in vitro. Sulfadiazine probably should be used in conjunction with penicillin, not only because of its inhibitory effect on the causative organism, but also because of its effect on the many other contaminating bacteria which are present. Surgical procedures will be indicated, varying with the extent of the lesion, the patient himself, and his response to drugs used in treatment. Adequate incision and drainage of abscesses are necessary. More radical procedures, such as resection of tubo-ovarian granulomas, may be indicated if there are recurrences after adequate treatment with penicillin and sulfadiazine.

Adequate follow-up data were available in 108 of our 122 cases of abdominal actinomycosis. The rate of cure in 73 cases in which penicillin or sulfonamides were not available for treatment was 16 per cent. In 13 cases in which adequate dosages of 1 of the sulfonamides were used the rate of cure or improvement was 38.7 per cent. In 24 cases in which adequate penicillin therapy was instituted the rate of cure or improvement was 95.8 per cent. As previously mentioned, adequate dosages of both penicillin and sulfonamides were used in 1 case. Strenuous dietary and supportive therapy, as well as surgical procedures, were utilized in all cases.

The prognosis in abdominal actinomycosis has greatly improved with recent advances in therapy.

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TRACHEOTOMY IN THE MANAGEMENT OF SEVERE HEAD INJURIES

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ALTHOUGH it is generally agreed that maintenance of an almost perfect airway is of supreme importance in patients unconscious from head injuries,[1,2] the use of tracheotomy for this purpose has been neglected. The airway is of first importance because of its aid in the prevention of cerebral anoxia, a devastating sequel to craniocerebral trauma. Whereas anoxia may be due to anemia produced by loss of blood, shock, or increased intracranial pressure, it most commonly follows secretional respiratory obstruction. To provide proper aeration of the lungs and thereby prevent this common cause of anoxia the following measures are in general use at the present time in most hospitals: (1) rubber oral airway which holds the tongue forward; (2) lateral position of the patient with intermittent elevation of the foot of the bed so that secretions in the tracheobronchial tree may drain from the mouth by gravity; (3) urethral catheter to aspirate secretions from the pharynx, larynx, trachea, and bronchi; (4) oxygen by nasal catheter, mask, or oxygen tent; (5) aspiration of the tracheobronchial tree through a bronchoscope; and (6) endotracheal tube for periods up to 48 hours. Although 1 or more of these measures suffice in the majority of cases of head injury, we recently became convinced that more attention to the respiratory requirements of the severely injured is needed if the mortality is to be lowered.

Tracheotomy apparently has been rarely used in the management of patients with head injuries. Not a single case report describing its use could be found in a survey of the recent medical literature and only 5 references[3-7] were found in which tracheotomy was mentioned as a possible method of solving the respiratory problems of such patients. On the other hand, for several years tracheotomy has been coming into general use in the postoperative care of certain patients with brain tumors. A small percentage of such patients may remain unconscious or stuporous for days, during which time they make little effort to keep their lungs dry by coughing. Others have depression of coughing and swallowing reflexes, or disturbed respiratory centers following removal of tumors of the posterior fossa which have been compressing the brain stem. Horrax[8] and Poppen[9] advocated tracheotomy after removal of acoustic neuromas if respiratory complications develop. McKenzie,[10] who employs tracheotomy postoperatively on patients with all types of brain tumors who have respiratory complications, strongly recommended its use. Recently, Parhad and Horrax[11] reported a case in which utilization of tracheotomy made possible a favorable outcome after removal of a cerebral abscess.

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The first tracheotomy on our service was performed Dec. 28, 1947, on a patient comatose from encephalitis; to date on 2 of our hospital services (Charity Hospital in New Orleans and Ochsner Foundation Hospital) we have used tracheotomy for relief of respiratory difficulties with gratifying success in 25 patients with nontraumatic conditions, including such lesions as brain tumor, cerebral abscess, meningitis, aneurysm, and apoplexy.

Tracheotomy, of course, has had varied applications in nonneurosurgical fields.[12,13] Even so, new indications are appearing. Galloway and Seifert[14,15] reported favorable results in bulbar poliomyelitis when tracheotomy was used to prevent respiratory obstruction by secretions. Creech, Woodhall, and Ochsner[16] reported the effectiveness of tracheotomy in decreasing the mortality of tetanus. Cardon[17] recently emphasized the benefits derived from tracheobronchial aspiration of retained secretions in a host of medical conditions. He mentioned tracheotomy in patients who, because of continued coma, require aspiration for prolonged periods.

In order to determine the status of tracheotomy in other fields, we classified all tracheotomies done at the Ochsner Foundation Hospital since its opening Jan. 1, 1947, to July 1, 1950. Of 108 patients having tracheotomies during this period, 39 were on the otolaryngologic service, 44 the general surgical service, and 25 the neurosurgical service. Of the entire 108 patients only 39 had tracheotomies because of obstructive lesions, such as carcinoma of the larynx, paralysis of the vocal cords, or membraneous croup. The remaining 69 patients had no laryngeal pathologic condition, and this procedure was done solely to prevent or correct respiratory complications. It was interesting to find that of these 69 patients tracheotomy was done as an emergency procedure after respiratory complications arose in only 32 patients, whereas it was performed purely as prophylaxis against respiratory complications after major operative procedures in 37 patients. It is apparent that tracheotomy is being used more frequently to prevent as well as to treat respiratory complications of numerous surgical conditions.

Between Jan. 27, 1948, and July 1, 1950, tracheotomy was performed (by a laryngologist when available) on 15 patients who had serious respiratory complications following severe craniocerebral trauma. The advantages of tracheotomy over other methods of providing an airway as observed in these patients comprise this report.

OBSERVATIONS ON PATIENTS WITH HEAD INJURIES

Before Tracheotomy.—Our observations are strictly clinical in that no attempt has been made to determine the effects of tracheotomy on such factors as the oxygen saturation of the arterial blood, the carbon dioxide content of the blood, or the pressure in the jugular veins. Clinically, these respiratory problems are fairly stereotyped during the first few hours following injury, varying only slightly from patient to patient. Breathing through the mouth is the rule, the nasal passages being closed by traumatic edema and inspissated mucus. The tongue, usually swollen, tends to fall posteriorly to cause partial occlusion of

the pharynx. Hematomas about the neck, when present, further encroach upon the pharynx, particularly if the mandible or hyoid bones have been fractured. Saliva, which is greatly increased in amount, supplemented perhaps with blood and cerebrospinal fluid, pools in the hypopharynx and runs down into the trachea. To this overabundance of fluid is sometimes added vomitus, particularly in alcoholic patients and children. These fluids are augmented further by tracheobronchial secretions, which are increased in amount, as is salivation, presumably by vagus stimulation. The respiratory rate is usually increased, inspiration being accompanied by stertorous bubbling noises. The muscular effort associated with breathing may lead to indrawing about the sternal notch and supraclavicular spaces of the neck. On auscultation of the chest one hears loud bronchial breath sounds and bubbling râles throughout, the forceful inspiration and recoil expiration doing little more than moving air back and forth in the bronchial tree. The patient is unable to swallow or does so infrequently. An effectual cough mechanism is likely to be absent even though the patient may respond to painful stimuli. Those patients restless enough to require sedation or restraints often seem oblivious to the pharyngeal and tracheal secretions, whereas a stuporous patient may remain so for days before respiratory complications develop because the coughing and swallowing reflexes are present, however inefficient. A comatose patient, on the other hand, may become a problem of progressive asphyxia in a matter of hours. Moderate cyanosis may occur from time to time, but loss of blood and shock may prevent it from appearing.

Patients with depression of the respiratory center have another type of respiratory difficulty. This type of respiration is characterized by slow (5 to 12 a minute), shallow respiratory excursions obviously associated with poor aeration of the lungs. Inspiration and expiration are both of short duration. The inspiratory movements are not forceful and the patient is quiet. The mandible is usually depressed on inspiration and the head extended slightly, both movements being devoid of force. Cheyne-Stokes respirations may precede the onset of this type of inadequate breathing. Mild cyanosis is often present although circulatory failure may prevent it from appearing.

After Tracheotomy.—The respiratory improvement after tracheotomy is usually dramatic. This is true in spite of the pretracheotomy use of an oral airway, nasal oxygen, tracheal suction, and other common methods of attempting to maintain an adequate airway. Following tracheotomy the noisy and labored breathing instantly disappears, the respiratory rate approaches normal, and the respiratory movements become natural and efficient. The patient looks better and seems relaxed, once freed of the muscular effort associated with breathing. The tracheobronchial tree can be quickly and easily emptied of excessive secretions by the insertion of a catheter through the tracheotomy tube. The tracheal suction apparatus can be turned over to the nurse, with periodic supervision, with the assurance that the assignment is simple and will be used as often as necessary. The patient can be turned frequently and the head of the bed elevated, as postural drainage is no longer required. The possibility of aspiration

of vomitus is no longer a concern. The assurance that the patient will be free of respiratory complications as a result of the injury for the coming desperate days or weeks is a relief to all concerned.

EXPERIENCE WITH TRACHEOTOMY IN 15 PATIENTS WITH HEAD INJURIES

Tables I and II present our experience with 15 patients who had tracheotomies after severe head injuries. These 15 cases represent approximately 10 per cent of patients with important head injuries treated during the same period. None had significant associated thoracic injuries. The interval between injury and tracheotomy depends, of course, upon the need in the individual case, as indicated by such factors as associated injuries, necessity of operative procedures, and failure of other methods to provide an adequate airway. Eight of the 15 patients in this series required neurosurgical procedures. Débridement of the brain was performed in 2 cases. There was 1 case each of subdural hematoma, intracerebral hematoma, and bilateral subdural hydroma. There were 3 cases of negative trephination for suspected hematoma.

Table I presents a brief analysis of the 9 tracheotomized patients who survived. The average age for this group is 23 years. Tracheotomy was performed on an average of 6.4 hours after injury in 7 of the patients and 96 hours after injury in the remaining 2. Six had some type of craniotomy. All but 2 of the patients remained unconscious for more than 4 days. The average period of unconsciousness in 8 of the patients was 15 days. One patient was still unconscious and continued to demonstrate decerebrate rigidity when transferred to another hospital several weeks after injury. In 8 of the patients the tracheotomy was closed in from 4 to 23 days after consciousness was regained. One patient was transferred to another hospital with the tracheotomy tube still in place. The fact that all but 2 of the patients were unconscious for more than 4 days indicates the severity of the injury in this group and confirmed our clinical impression that these patients would require aid for a long time in maintaining an adequate airway. The tracheotomies were closed only after each patient could be fed by mouth and could maintain his tracheobronchial toilet 24 hours a day. We believe that the majority of these patients would have died had reliance been placed upon a method of maintaining an adequate airway other than tracheotomy.

Table II presents pertinent data on the 6 patients who died of severe head injuries without regaining consciousness. Their average age is 54 years as compared with 23 for the group of survivors. Patient 14 died 1 hour after tracheotomy of contusions of the cerebral hemispheres and brain stem. The absence of cyanosis in this patient was probably due to concurrent circulatory failure; the lungs were normal at necropsy. He would obviously have done as well with an endotracheal tube. It is difficult, however, to predict which patients will survive until their response to the use of an endotracheal tube or tracheotomy has been observed. The presence of extensive damage to the medullary respiratory center may explain failure of tracheotomy to restore normal breathing, a bad prognostic sign. Also, patients may die of respiratory failure despite tracheotomy if there is interference with the alveolar gas exchange, as in patients with thoracic injuries or pulmonary edema of cardiac origin. Two deaths in the group were not

TABLE I. TRACHEOTOMY IN NINE PATIENTS SURVIVING SEVERE HEAD INJURIES

PATIENT	AGE (YEARS)	TRACHEOTOMY PERFORMED (HOURS AFTER INJURY)	OTHER OPERATIONS	DURATION OF COMA IN DAYS	TRACHEOTOMY CLOSED (DAYS AFTER INJURY)	CONDITION ON DISCHARGE
1. E.A.	26	15	Débridement of brain	2	14	Ambulatory
2. V.B.	43	3	None	5	14	Ambulatory
3. G.P.	8	5	Negative trephines	17	21	Ambulatory
4. P.D.	41	96	None	26	29	Ambulatory
5. L.M.	28	7	None	6	11	Hemiplegic
6. J.D.	8	2	Débridement of brain	1	17	Ambulatory
7. L.T.	2	96	Removal intracerebral hematoma	34	48	Hemiplegic
8. F.B.	21	5	Removal subdural hematoma	31	54	Disoriented
9. W.O.	30	8	Negative trephines	90+		Decerebrate

TABLE II. TRACHEOTOMY IN SIX PATIENTS WITH FATAL HEAD INJURIES

PATIENT	AGE (YEARS)	TRACHEOTOMY PERFORMED (HOURS AFTER INJURY)	OTHER OPERATIONS	TIME OF DEATH AFTER INJURY (HOURS)	CAUSE OF DEATH
10. C.B.	38	72	Drainage bilateral hydroma	168	Anuria
11. A.S.	66	4	Negative trephine	96	Apoplexy
12. C.T.	15	6	None	72	Midbrain and cerebral contusions
13. E.J.	60	3	None	18	Brain stem laceration
14. W.M.	59	3	None	4	Brain stem and cerebral contusions
15. O.M.	86	5	None	24	Cardiac failure

directly attributable to respiratory failure. Patient 10 died of renal insufficiency on the eighth day and patient 11 of apoplexy on the fourth day, both showing no evidence of respiratory complications either during life or at necropsy. The remaining 3 patients, as was true of Patient 14, had inadequate respiratory exchange at the time of death despite tracheotomy. Patient 12, who had shallow, ineffectual respirations with cyanosis despite tracheotomy and the administration of oxygen, died of midbrain and cerebral contusions 3 days after injury. The lungs were normal at necropsy. Patient 13 died from a bullet wound of the brain stem after 15 hours of cyanosis in spite of the continuous administration of oxygen through the tracheotomy cannula. At necropsy there was no pulmonary disease. Case 15, the third patient with inadequate respiratory exchange at the time of death, despite tracheotomy, died 19 hours after tracheotomy of cardiac failure and pulmonary edema. Almost continuous tracheal suction was required to remove the fluid accumulating in the large bronchi; the lungs were extremely edematous at necropsy, a fact which accounts for the patient's cyanosis.

REPORT OF CASES

CASE 1.—E. A., a 26-year-old man, was admitted to Charity Hospital in New Orleans in deep coma after an automobile accident. In addition to a compound depressed fracture of the skull from which oozed blood and fragments of brain, he had multiple compound fractures of the facial bones, an extensive compound fracture of the mandible, and simple fractures of 1 clavicle and several ribs. Pharyngeal suction, an oral airway, and oxygen by catheter improved the rapid (50 to 60 a minute) respirations; however, in a few hours extreme muscular effort became associated with breathing. Swelling of the tongue and neck all but occluded the pharynx in spite of the oral airway. The secretions became tenacious and difficult to remove by suction. Loud bubbling râles were heard throughout the lungs. Breathing would cease entirely whenever the neck was hyperextended in an effort to pass a catheter into the trachea. Tracheotomy was performed 15 hours after injury, following which a large amount of secretions was removed by suction with complete relief of the previous respiratory obstruction. The brain was débrided and the compressed skull fracture elevated 15 hours after the tracheotomy. Although consciousness returned 2 days after injury, oxygen was needed for 6 days. Tracheobronchial secretions were removed for 10 days, as the patient refused to cough because of pain. The fractured mandible made tube feeding necessary. The tracheotomy was closed 14 days after the injury and the patient was sent home.

CASE 2.—V. B., a 43-year-old man, was admitted to Charity Hospital in a semicomatose state following a head injury. He was restless and made constant efforts to get off the stretcher. Blood and spinal fluid trickled from the right ear and a large subcutaneous hematoma extended from the right temporal area in the neck. Facial paralysis was noted on the right side. Respirations were rapid, noisy, and labored. Despite restraints an oral airway could not be kept in place; postural drainage proved to be unsatisfactory. Pharyngeal suction was difficult and endotracheal suction impossible because of the patient's struggling. Following performance of a tracheotomy 3 hours after the injury, the secretions in the tracheobronchial tree were removed with ease, the respirations became effortless, and restraints were no longer required. It was soon evident from the progressive improvement following establishment of an adequate airway that the patient would need no further operative procedures. Oxygen was required for 5 days and suction was used innumerable times even after the patient regained consciousness. The tracheotomy was closed 2 weeks after admission and the patient was ambulatory on discharge.

CASE 3.—G. P., an 8-year-old boy, was admitted to Charity Hospital after 2 hours of semiconsciousness due to a blow in the head. Hemiplegia was present on the right side of the body and violent extensor spasm occurred every few minutes on the left side. The noisy, labored respiration improved somewhat after pharyngeal suction. An oral airway and oxygen by catheter were provided. Shortly afterward the left pupil became dilated, an observation leading to bilateral trephination which revealed contusions of the cortex. A prophylactic tracheotomy was immediately performed because it was realized that the child would probably remain unconscious for days. There were no respiratory complications during the following 17 days of stupor despite the presence of a stomach tube. Tracheal suction was required repeatedly, as the patient made no effort to cough. When last seen 4 months later there was mild aphasia, the right hemiplegia had partially disappeared, and the patient was able to walk.

CASE 4.—P. D., a 41-year-old man, was admitted to the Ochsner Foundation Hospital after 24 hours of semiconsciousness due to a head injury. Breathing was labored and stertorous; the rate was 40 a minute. Pharyngeal suction removed much bloody mucus and after the placement of an oral airway and the administration of oxygen, the patient appeared greatly improved. The following day, after a stomach tube had been inserted for feeding purposes, the respirations again became loud and labored, and mild cyanosis was detected. The patient improved for short periods following vigorous attempts to clear the airway by endotracheal suction; however, sedatives and restraints became necessary because of restlessness. On the second day of hospitalization the tube feedings were discontinued and an endotracheal tube was inserted by an anesthetist. Despite repeated suction through the endotracheal tube the patient was soon experiencing rapid, labored respirations with episodes of cyanosis. The endotracheal tube was removed the next day and a tracheotomy was performed. Despite the following 22 days of stupor the patient experienced no further respiratory problems. Tracheobronchial suction was necessary during this period; feeding was accomplished entirely through a stomach tube. Had tracheotomy been performed earlier this patient would have been spared 2 days of recurring respiratory distress. A state of mental depression delayed his leaving the hospital until several weeks later.

CASE 5.—L. M., a 28-year-old man, was admitted to Charity Hospital after 6 hours of coma following an accidental gunshot wound of the head. The wound, from which blood and cerebrospinal fluid drained continually, was located directly beneath the left eye. A roentgenogram of the skull revealed metal fragments in both cerebral hemispheres. There was complete hemiplegia on the right side; aphasia became evident when the patient regained consciousness. Tonic convulsive movements followed by extensor spasm occurred on the left side. These movements, lasting several minutes at a time, were violent and accompanied by infrequent gasping respirations. The breathing between convulsive movements was labored, noisy, and rapid with indrawing of the skin of the neck. Tracheal rattles and loud bubbling râles were heard throughout the lungs. The lips and nails were cyanotic and it seemed as if the patient would die any minute. An oral airway, nasal oxygen, pharyngeal suction, and attempts at postural drainage did not help appreciably. Attempts to pass a catheter into the trachea were

unsuccessful because of the convulsive movements. Tracheotomy was performed 7 hours following injury after which the retained secretions were easily removed and the difficulty in breathing disappeared. The convulsive movements immediately became less violent and ceased entirely 1 hour later. Six days of deep coma ensued after which the patient would follow a light with his normal eye and squeeze fingers with his left hand on command. On the eleventh day the spinal fluid drainage ceased and the tracheotomy was discontinued, as the patient could cough and take nourishment by mouth. At the time of discharge 5 weeks later the patient could talk but was hemiparetic.

CASE 6.—J. D., an 8-year-old girl, was admitted to Charity Hospital in a semiconscious state after being struck by a bus. A compound fracture of the frontal bone caused herniation of the lacerated left frontal lobe. Her struggling accentuated the tendency of the brain to herniate. A tracheotomy was performed, followed by débridement and repair of the wound. The patient could talk the following morning and was eating a soft diet on the third day. Removal of the tracheotomy tube was delayed because she could not be persuaded to cough. Her improvement by the seventeeth day was sufficient to permit removal of the tracheotomy and when last seen 1 year later a small pulsating defect of the scalp was apparently the only residual.

CASE 7.—L. T., a 2-year-old boy, was admitted to Charity Hospital following a fall from a third story window. The patient was in a coma; the pupils were fixed, and the right one was dilated. Brain herniated through a wound of the right temporal region, and hemiplegia was present on the left side. After correction of shock a large intracerebral hematoma was removed. Oral suction was employed and oxygen was given through a nasal tube postoperatively with only moderate success. Episodes of cyanosis and noisy respirations occurred but could be relieved by vigorous pharyngeal suction. Tube feeding accentuated these episodes. On the fourth day, considerable indrawing of the skin over the supraclavicular spaces and intercostal interspaces appeared. The respirations were gasping, and loud, bubbling râles were heard throughout the lungs. Further suction did not improve the patient, who at this time was in deeper coma than on admission. Tracheotomy was performed, after which breathing became regular and the temperature and pulse rate returned to normal. Despite 30 more days of coma, during which time the patient was fed through a tube, no further respiratory complications arose. The tracheotomy was closed after 48 days. When last seen 18 months after the initial injury he could stand with support.

CASE 8.—F. B., a 21-year-old man, was admitted to Charity Hospital in deep coma following a fall. The patient was completely unresponsive and without reflexes. Dilatation of the left pupil led to trephination of the skull. A subdural hematoma was removed; in addition severe cerebral contusion was apparent. Tracheotomy was performed at the end of the operation. The deep coma continued. Other exploratory trephines gave negative results. One month later the patient could perceive light and 54 days after injury the tracheotomy could be discontinued even though tube feedings were still required. Although still disoriented he was transferred to a convalescence hospital about 3 months after injury.

CASE 9.—W. O., a 30-year-old man, was admitted to the Ochsner Foundation Hospital 6 hours after an automobile accident. The pupils were unequal and the patient unresponsive. The breathing was forceful, with indrawing of the skin of the neck. Bilateral trephines revealed only contusion of the brain. Tracheotomy was performed immediately after the operation. The patient continued to demonstrate decerebrate rigidity and was transferred 90 days later to another hospital. There were no respiratory complications during this period.

DISCUSSION

Practically every patient with a severe head injury is in danger of partial respiratory obstruction from pharyngeal and tracheal secretions. The labored breathing required to overcome this partial respiratory obstruction causes elevation of the intrathoracic venous pressure. The increased intrathoracic pressure

is readily transmitted to the intracranial venous system, leading to venous congestion of the brain and elevation of the intracranial pressure. It is well established that pronounced elevations of intracranial pressure may result by this mechanism. Also, partial respiratory obstruction by retained secretions may lead to elevation of the carbon dioxide content of the systemic and cerebral arterial blood. Arterial blood of high carbon dioxide content is the most potent local vasodilator of the cerebral vessels that is known to exist.[18-23] In addition, the deficient airway may lower the oxygen content of the arterial blood. When the cerebral vascular endothelium becomes sufficiently anoxic, it is permeable to fluids and to erythrocytes with resulting edema and hemorrhagic tendency. Arterial blood of low oxygen content is also a local vasodilator of the cerebral vessels, although not as potent a dilator as arterial blood with an elevated carbon dioxide content.[18-23]

Partial respiratory obstruction may lead, therefore, to intracranial venous congestion and active vasodilatation of the cerebral vessels. Both venous congestion and arterial dilatation raise the intracranial pressure. Both also encourage bleeding from vessels already damaged by the cerebral trauma. Intracranial bleeding further elevates the intracranial pressure, which, in time, depresses the medullary respiratory center, leading to accentuation of the deficiencies in the airway and decreased aeration of the lungs. In this manner a vicious cycle is established. By preventing additional damage to the traumatized brain by these mechanisms, an adequate airway may shorten the period of coma, lessen the residual neurologic deficit, and save the patient's life in a number of instances. The insidious nature of the damaging sequels of an inadequate airway has often erroneously caused the head injury to be held responsible for the patient's continued stupor and difficult breathing. Also, the cerebral damage from anoxia, manifested as deepening coma, decreasing pulse rate, and rising blood pressure, is often attributed incorrectly to the primary injury. Furthermore, absence of cyanosis does not mean the patient's airway is adequate. Cyanosis, in fact, is often late in appearing even though anoxia sufficient to damage cerebral tissue has been present for hours.

Still another factor may be listed in which the deficient airway so common to patients with severe head injuries may be harmful. The muscular effort associated with the labored breathing required to overcome the partial respiratory obstruction may lead to exhaustion of the patient. The existing anoxia leads to restlessness which further increases the demands of the body for oxygen. A restless individual struggling for air is indeed the antipathy of the resting state so important for these patients. Also, sedation for restlessness has contributed to the anoxic state by depressing the central respiratory center.

An adequate airway may be obtained in patients with severe head injury by endotracheal intubation or tracheotomy. The other methods in common use are inadequate or difficult to maintain in patients with severe head injuries who have serious respiratory problems. Endotracheal intubation and tracheotomy allow instant and repeated tracheal suction as well as the administration of oxygen. Since both methods by-pass the pool of secretions present in the hypopharynx, pneumonia from aspiration is prevented and feeding by stomach tube

in safe. This is not true of endotracheal intubation, however, unless a cuffed tube properly inflated is employed. The use of an endotracheal tube is indicated in those cases in which the respiratory difficulty is likely to be resolved in 12 to 20 hours. Its use for longer periods is unsatisfactory, as the diameter of the lumen becomes lessened by layers of inspissated mucus, and edema of the larynx may make re-intubation difficult or impossible. Also, the trauma of repeated intubation and the continuous pressure exerted by the indwelling tube may lead to unavoidable ulcerations of the upper respiratory pathways should the endotracheal tube be used for long periods of time. Tracheotomy should be performed when the respiratory difficulty can be expected to last for more than 24 hours. For a given case it may be difficult to choose between the 2 methods at the time of the patient's admission to the hospital. In such cases an endotracheal tube may be used for the first 24 hours and at the time of its removal tracheotomy can be performed should the respiratory problem persist. We have found it practical, however, to perform tracheotomy initially if doubt arises as to the method of choice. This is especially true in patients with injury of the maxillofacial structures or nasopharynx, as endotracheal intubation may be hazardous in such cases.

The occasional failure of a patient to regain adequate respiratory exchange after tracheotomy may be due to a disturbance of the acid base equilibrium, uremia, traumatic hemothorax, traumatic rupture of the lung, pneumothorax, exsanguination, pulmonary edema, or damage to the respiratory center. Before it is assumed that a damaged respiratory center is responsible for a deficient exchange after tracheotomy, a careful search should be made to exclude the other possible causes.

CONCLUSIONS

Tracheotomy is superior to any other method of maintaining efficient aeration of the lungs in unconscious patients. It should be performed promptly and unhesitantly in every patient unconscious from a head injury if it seems likely that the coma will persist more than 24 hours and if nonsurgical methods of maintaining an adequate airway appear to be inefficient.

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DISINFECTING ACTION OF pHISODERM CONTAINING THREE PER CENT HEXACHLOROPHENE ON THE SKIN OF THE HANDS

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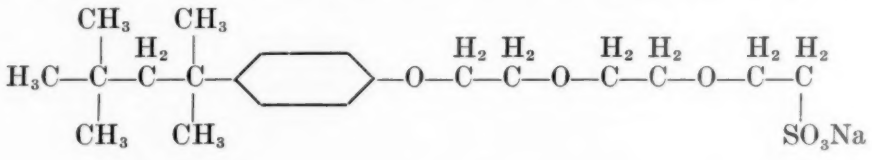
SKIN disinfection is a recurring problem to the surgeon interested in advancing surgical technique. Most germicides have been fostered in the hope that a single application would suffice to disinfect the skin. Price[1] demonstrated that mechanical cleansing alone removed bacteria and that quantitative recovery of the normal flora of the skin required several days. Traub, Newhall, and Fuller[2] demonstrated that it is possible to suppress the bacteria and thereafter maintain an exceedingly low bacterial flora on the skin by the daily use of soap containing hexachlorophene.‖ Bacteriologically, safe hands are therefore practicable among hospital personnel.

A previous report by Hufnagel, Walter, and Howard[3] furnishes details of an in vivo technique for investigation of skin disinfection. Observations on the bactericidal action of coconut oil soap, aqueous Zephiran solution, and pHisoderm have been published. Preliminary work on the effectiveness of pHisoderm, a skin detergent containing 3 per cent hexachlorophene, an antibacterial agent, was sufficiently promising to prompt the present study to discover the logical technique for using this new germicide in surgical practice. Previous studies on hexachlorophene concern themselves with its bactericidal activity in an alkaline medium such as is found in soap. A detergent other than soap is essential as the vehicle for the germicide because many surgeons suffer contact dermatitis from the use of soap. This report offers evidence that hexachlorophene is also effective in an acid detergent medium that is hypoallergenic.

NATURE OF AGENTS TESTED

pHisoderm is a water-miscible anionic detergent cream containing a sulfonated ether, wool fat cholesterols, lactic acid, and petrolatum. It is a stable



Sodium octylphenoxyethoxyethyl ether sulfonate, "Triton 720"

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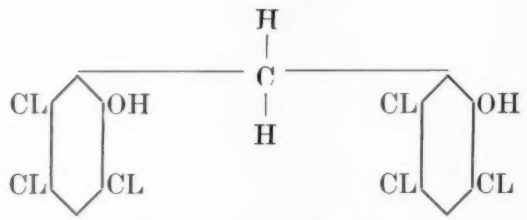
‖Hexachlorophene is the name accepted by the Council on Pharmacy and Chemistry in lieu of the original and popular name G-11.

mixture which does not hydrolyze to form sulfuric acid and is reported to be 40 per cent more active than ordinary soaps in depressing the surface tension of water and in deflocculating and dispersing soil. It is an active emulsifier to all types of oils and produces suds with very little friction. It contains neither perfume nor coloring matter. The pH value is 5.5, corresponding to that of normal skin, hence its trade name "pHisoderm." It is hypoallergenic and, unlike soap, it retains its detergent and sudsing properties in all kinds of water, including sea water, regardless of temperature.[4]

Hexachlorophene is a bactericidal synthetic diphenol with the formula:



bis (2 hydroxy-3,5,6-trichlorophenyl) methane

It is prepared as a white crystalline material with a melting point of 164 to 165° C. It also is hypoallergenic[5] and relatively nontoxic. Solubility data are given in Table I.

TABLE I. SOLUBILITY OF HEXACHLOROPHENE

SOLVENT	GM. OF HEXACHLOROPHENE DISSOLVED IN 100 C.C. AT 25° C.
Water	0.0012
10% ethyl alcohol	0.013
20% ethyl alcohol	0.02
50% ethyl alcohol	0.15
75% ethyl alcohol	4.94
Propylene glycol	24.5
Isopropyl alcohol	31.6
Methyl ethyl ketone	77.0

In studies on the comparative bactericidal activity of these 2 materials, carried out by the agar cup-plate method against *Staphylococcus aureus*, pHisoderm displayed a 1 mm. zone of inhibition. With pHisoderm containing 3 per cent technical hexachlorophene, there was a 12 mm. zone of inhibition. This compares favorably with corresponding studies on mercurial salt and quaternary ammonium salt compounds. Phenol coefficient studies (Table II) further illustrate that the pHisoderm and hexachlorophene mixtures are effective in low dilutions.

LABORATORY METHOD

Details concerning the mechanical scrubber employed and the techniques of scrubbing, of collecting samples, and of plating cultures, are described in the previous publication.[3] A pressure of 110 Gm. was exerted on the brush in all scrubs, both to the skin of the palm and of the back. In an effort to minimize the growth of colonies of spreading organisms which nullified the findings of many previous experiments in this series, Difco tryptase nutrient agar culture

TABLE II. PHENOL COEFFICIENTS* OF pHISODERM AND HEXACHLOROPHENE

AGENT TESTED	DILUTION	RESULT OF CULTURE TRANSFERRED AT END OF INTERVAL OF MINUTES			PHENOL COEFFICIENT
		5	10	15	
Phenol standard	1:60	+			
	1:70	+	+	+	60
	1:80	+	+	+	
pHisoderm control	1:40	+	+	+	
	1:60	+	+	+	
	1:80	+	+	+	
pHisoderm+ 0.25% hexachlorophene	1:40	+	+	+	
	1:60	+	+	+	
	1:80	+	+	+	
pHisoderm+ 0.5% hexachlorophene	1:40	+	+	+	
	1:60	+	+	+	
	1:80	+	+	+	
pHisoderm+ 1% hexachlorophene	1:40	+			
	1:60	+	+	+	$\frac{40}{60} = 0.6$
	1:80	+	+	+	
pHisoderm+ 3% hexachlorophene (technical)	1:40				
	1:60				$\frac{150}{60} = 2.5$
	1:80				
	1:100				
	1:200	+	+		
pHisoderm+ 3% hexachlorophene (purified)	1:40				
	1:60				
	1:80	+	+		$\frac{150}{60} = 2.5$
	1:100	+			
	1:200	+	+	+	
pHisoderm+ 5% hexachlorophene	1:40				
	1:60				
	1:80				$\frac{150}{60} = 2.5$
	1:100				
	1:200	+	+		

*Phenol coefficient is a figure obtained by dividing the numerical value of the greatest dilution of the disinfectant capable of killing *Eberthella typhi* in 10 minutes, but not in 5 minutes, by the greatest dilution of phenol showing the same result.

medium was employed. Pour plates were incubated at 37° C. and total colony counts were recorded after 48 hours incubation employing a Quebec colony counter.

Volunteer subjects were selected at random from college students, medical students, and laboratory personnel. All were requested not to wash their hands for 4 hours before the test and none had used germicidal solution for 4 days.

Of 236 individual scrubbing experiments, 119 were considered satisfactory for statistical evaluation. The remainder were discarded because of spreaders or because of the fact that too few organisms were obtained to give accurate curves. Many of these experiments were run before the persistent effect of hexachlorophene on the skin was fully appreciated. Experiments with initial counts of over 100 colonies per cubic centimeter showed sufficient differential for tabulation purposes. Table III indicates the distribution of satisfactory scrubs over the several experimental series.

TABLE III. IN VIVO EFFECT OF VARIOUS DETERGENTS

AGENT	CONTROL WATER	pHISODERM NO. 44 AND WATER āā	50% SOLUTION pHISODERM & 1.5% HEXACHLOROPHENE	10% SOLUTION pHISODERM & 0.3% HEXACHLOROPHENE	5% SOLUTION pHISODERM & 0.15% HEXACHLOROPHENE
NUMBER OF EXPERIMENTS	25	9	6	24	36
SCRUB PERIOD	AVERAGE NUMBER OF COLONIES GROWN FROM WASHINGS OF EACH SCRUB PERIOD				
1	814.0	2037	674	814	2413
2	317.5	----------	----------	agent applied	----------
3	173.5	----------	----------	water discarded	----------
4	116.3	4.4	9.6	0.64	0.5
5	100.9	5.0	0.8	0.32	0.91
6	35.9	11.4	1.1	0.36	0.8
7	40.0	5.3	0.6	0.32	0.47
8	30.6	3.5	1.8	0.72	0.42
9	23.8	5.6	4.0	0.68	0.51
10	23.2	3.9	2.8	0.3	0.51
11	16.1	3.4	3.1	0.4	0.5
12	11.5	4.6	2.5	0.76	0.57
13	8.7	4.3	2.6	0.20	0.44
14	20.5	3.6	2.0	0.48	0.36
15	4.8	3.5	3.3	0.20	0.55
16	6.9	5.7	1.8	0.52	0.28
17	6.1	2.4	1.5	0.64	0.70
18	5.1	4.4	0.3	0.48	0.38
19	3.9	4.6	1.5	0.68	0.36
20	2.8	7.3	1.1	0.48	0.86
21	4.4	6.1	1.1	0.24	0.44
22	4.5	3.9	1.8	0.64	0.49
23	4.0	3.6	1.1	0.48	0.44
24	3.0	3.2	1.5	0.68	0.83
25	3.4	2.2	1.0	0.56	0.47
26	2.6	3.0	1.6	0.52	0.55
27	2.9	1.5	1.6	0.2	0.28
28	5.1	2.2	2.5	0.48	0.80
29	.2	4.4	2.5	0.4	0.91
30	.3	2.1	1.0	0.36	0.52

The data presented in Table III are illustrated in Fig. 1 where the bacterial colony counts have been plotted cumulatively to present a greater contrast on the graph for purposes of clarity. The number indicated at any point on the curve means the total number of organisms yet to be removed by subsequent scrubbing. The control curve using distilled water indicates the effectiveness of mechanical removal of bacteria. The other curves illustrate the antibacterial action of the various agents when applied to the moistened skin by 10 standard brush strokes over a maximum period of 1 minute. The detergent action of pHisoderm and of soap in increasing the efficacy of mechanical scrubbing is apparent. The antibacterial effect illustrated is assumed to be bactericidal rather than bacteriostatic, or exclusion by film formation, because during each experiment: (a) Each of twenty-eight subsequent periods of scrubbing with 5 c.c. of sterile water showed no increase in the number of organisms removed, even though the dilution of germicide increased in successive periods. During the last period a minimal dilution of 5×10^{-30} was attained, assuming 0.1 c.c. residual at each period. (b) There was sufficient mechanical action (280 brush strokes after the exposure to the agent) to abrade a film.

The application of these data to the scrubbing of the hands necessitates consideration of 5 factors:

1. A standard brush must be used. The Pro-phy-lac-tic brush No. 157, when sterilized in saturated steam at 121° C. for 30 minutes, has 10 times more mechanical scrubbing effect when rubbed on the skin in its longitudinal axis than the brush used in these experiments. Thirty strokes of the hand brush exert the same mechanical cleansing action as the whole series of scrub periods depicted in the control curve obtained by scrubbing with distilled water.

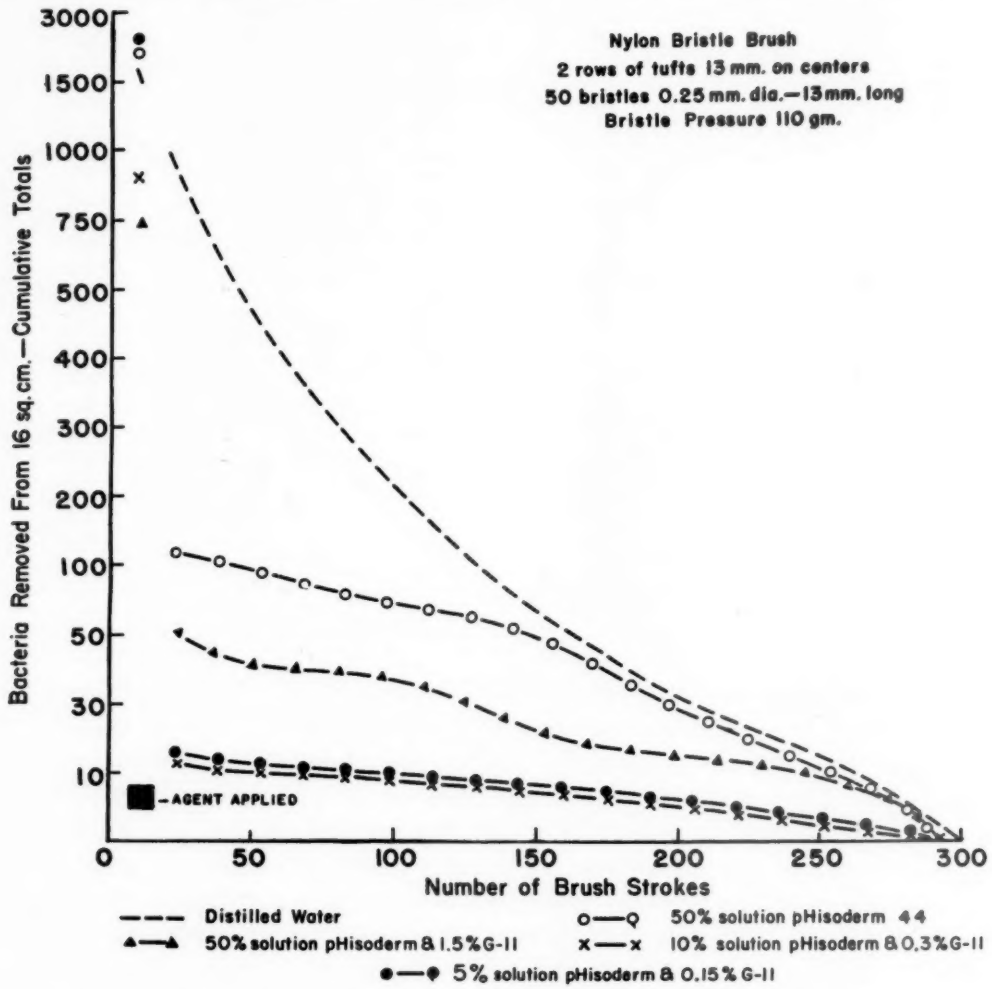


Fig. 1.—Disinfecting action of scrubbing detergents and germicides, showing the disinfecting action of pHisoderm containing 3 per cent hexachlorophene on the skin of the hands.

2. The mechanical scrub must be applied to every area of the skin to be disinfected. An anatomic scrub can be developed by following the technique described by Lilienthal.[6] Thirty brush strokes can be applied to the skin of both hands and forearms in 7 to 8 minutes by a diligent scrubber.

3. Enough detergent must be used to achieve maximum cleansing and bactericidal effect. One c.c. of pHisoderm containing 3 per cent hexachlorophene

with 10 c.c. of water added yield enough lather to cover the skin of both hands and arms. This lather contains 0.3 per cent hexachlorophene. Frequent rinsing and reapplication of the detergent mixture enhances its cleansing action.

4. The exposure to hexachlorophene which accomplished the bactericidal effect depicted in Fig. 1 can be multiplied 30 times by using it throughout the entire scrub. Small quantities of water should be added frequently to the lather during scrubbing to aid in solubilizing soil, which should be flushed away with the suds by frequent rinsing. Avoid adding more pHisoderm to the suds already on the skin or brush because it causes the breakdown of the detergent emulsion and interferes with cleansing.

5. The bacteriologic problem presented at each preoperative scrub can be estimated. A long interval between scrubs,[1] soiling of hands, particularly when accompanied by trauma, such as gardening, or other contamination of the skin will increase the bacterial flora and make disinfection more difficult. Daily scrubbing of a clean, smooth, intact skin depresses the bacterial flora so that the disinfection is more readily accomplished.

TABLE IV. SUPPRESSION OF BACTERIA AFTER DAILY WASHING

AGENT	SOAP AND WATER 3 TO 4 TIMES DAILY; NO WASHING FOR 4 HOURS PRIOR TO SCRUB		pHISODERM AND 3% HEXACHLOROPHENE DAILY FOR 1 TO 3 WEEKS; NO WASHING FOR 4 HOURS PRIOR TO SCRUB
NUMBER OF EXPERIMENTS	25		19
SCRUB PERIOD	AVERAGE NUMBER OF COLONIES GROWN FROM WASHINGS OF EACH SCRUB PERIOD		
1	814.0		38
2*	317.5		13.1
3	173.5		5.7
4	116.3		5.0
5	100.9		3.3
6	35.9		2.05
7	40.0		1.8
8	30.6		2.05
9	23.8		1.7
10	23.2		1.2
11	16.1		.8
12	11.5		1.1
13	8.7		.7
14	20.5		1.2
15	4.8		.9
16	6.9		.9
17	6.1		.6
18	5.1		.4
19	3.9		.8
20	2.8		.6
21	4.4		.6
22	4.5		.7
23	4.0		.9
24	3.0		.7
25	3.4		.6
26	2.6		.7
27	2.9		.5
28	5.1		.5
29	.2	(water control)	.3
30	.3	(agar control)	.3

*Ten c.c. sterile distilled water only used in each scrub period.

The staff members of the Peter Bent Brigham Hospital have been using pHisoderm containing 3 per cent hexachlorophene in preoperative scrubbing for 2 years. The technique used is as follows:

1. Use a Nylon bristle brush.
2. Scrape the subungual spaces with the sharp-edged tip of a stainless steel file.
3. Keep the nails trimmed to 1 mm.
4. Wet the hands and arms and brush thoroughly. Use the detergent sparingly; 2 c.c. will suffice for disinfection. Apply germicide and rinse off lather frequently.
5. Develop an anatomic scrub so that every area of the skin receives the following number of brush strokes (lengthwise of the brush):
   a. Those who scrub at intervals of more than 3 days, 30 brush strokes to the skin, 50 to the nails.
   b. Those who scrub daily, 15 strokes to the skin, 25 to the nails.
   c. Those who use pHisoderm with 3 per cent hexachlorophene routinely for washing the hands, 9 strokes to the skin, 15 to the nails.
6. Rub the hands and arms while immersed in 1-1000 aqueous solution of Zephiran for 2 minutes.

Scrubbing experiments done with sterile distilled water following this routine grew only occasional colonies. The technique was modified, therefore, to provide in vivo evidence of the effectiveness of the detergent by scrubbing the palms of the hands in the scrubbing machine 4 hours after simple washing with soap and water or pHisoderm containing 3 per cent hexachlorophene. These data are presented in Table IV. The suppression of the bacterial flora is obvious.

CONCLUSIONS

1. The relative effectiveness of a skin detergent (pHisoderm) in removing bacteria is contrasted with mechanical scrubbing with distilled water alone.

2. The disinfecting action of the detergent can be enhanced by the addition of hexachlorophene.

3. Hexachlorophene exhibits bactericidal action in the presence of an anionic detergent.

4. A routine preoperative scrub is described based upon the bacteriologic data.

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EXPERIMENTAL OCCLUSION OF THE SUPERIOR MESENTERIC VESSELS WITH SPECIAL REFERENCE TO THE ROLE OF INTRAVASCULAR THROMBOSIS AND ITS PREVENTION BY HEPARIN

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THE superior mesenteric vascular axis, maintaining the blood supply to the structures derived from the embryonal midgut, has in the past been considered an unalterable, inviolate pathway. Neoplasms invading this axis are ordinarily deemed unresectable, and accidental severance or occlusion of these vessels has regularly been disastrous. However, with the rapid advancement of vascular surgery in this and other areas that has occurred in recent years, it appeared fruitful to study in the laboratory means of circumventing this axis and still maintain vascular sufficiency of the midgut. As a foundation for such a venture it was first considered essential to study (1) the effects of occlusion of the main superior mesenteric artery and vein, (2) the length of time that flow in these vessels could be ablated, and (3) measures that might prolong the time that these vessels could be occluded. The results of these studies are to be presented in this report, and a later report will deal with attempts to reestablish intestinal circulation after severing the main superior mesenteric vessels.

LITERATURE

Scott and Wangensteen,[17] in 1932, performed a group of experiments on dogs to demonstrate the effects of occlusion of the blood supply to a loop of bowel. They found that when the arteries to a loop of bowel 1 to 5 feet in length were tied, death occurred in 15 to 24 hours. When arteries and veins were ligated, the animals died in 11 to 32 hours, and when the veins from a loop 3 to 3½ feet in length were tied, death followed in 2½ to 11½ hours. Emphasis was placed on the role of shock when the venous return from a long loop of bowel is occluded and to this is attributed the shorter survival time with venous occlusion. Laufman[8] found that after the superior mesenteric artery is occluded for 2½ hours there is secondary relaxation of the mesenteric vessels and the bowel viability is seriously impaired. He also found that when the superior mesenteric vein is clamped the animal dies in shock within 3 hours. Derr and Noer[5] claim no higher mortality with venous ligation than that when any other vessel or combination of vessels is ligated. In their experiments, however, a very short segment of bowel was devascularized so the effect of shock would be minimized.

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Cirrincione and Francona[3] demonstrated that when there is disturbance of the intestinal blood supply, there is an increased rate of absorption of bacteria into the blood stream. Measures designed to reduce bacterial growth in the bowel lumen should make it possible to deprive the intestine of its blood supply for longer periods of time without a fatal outcome. Sarnoff and Poth[14] and Sarnoff and Fine[15] pointed out that a course of Sulfasuxidine preoperatively reduced the mortality when the veins from a 50 cm. loop of ileum were tied. The mortality was 100 per cent in the controls but only 30 per cent for the animals that received the drug. Davis and associates,[4] using rabbits, devascularized 7.5 cm. lengths of bowel. They found that sufficient doses of streptomycin given subcutaneously preoperatively prevented mortality.

Martin, Laufman, and Tuell[12] in a recent paper stated that following experimental mesenteric venous occlusion, sludge appears in the small vessels within 10 to 20 minutes. Thrombus formation begins about 30 minutes later. They found that anticoagulants prevented thrombus formation in the presence of sludge by preventing sludged masses from sticking to the endothelial lining. Loewe and associates[11] tested the action of heparin on experimental venous thrombosis and found that in a heparinized animal early clots were resolved, the growth of a collateral venous channel was enhanced, and speedy recanalization occurred.

Much of the literature on experimental mesenteric vascular occlusion concerns interruption of the blood supply to a relatively short loop of bowel. Although sudden occlusion of the main superior mesenteric vessels is invariably fatal, Blalock and Levy[1] reported that gradual occlusion of the celiac and mesenteric axis over a period of 3 months was attended by some survivals, indicating that potential collateral channels are certainly present. Similarly, Laufman[7] gradually occluded the superior mesenteric vein, using cellophane bands, and observed the development of extensive collateral veins, with the intestine remaining viable. Also, Brunschwig[2] reported an instance in clinical material wherein the portal and superior mesenteric veins were ligated incidentally to removing a pancreatic carcinoma. Although the patient succumbed of peritonitis after 10 days, the intestine appeared quite normal and viable. In this unusual instance apparently collateral venous channels were sufficient to take over the venous load directly.

METHODS AND MATERIALS

Under pentobarbital anesthesia, a group of normal dogs was subjected to laparotomy. The abdomen was opened through an upper midline incision. Either the superior mesenteric artery, vein, or both were dissected out to their origin and occluded with a small rubber-shod clamp. The artery was clamped close to its origin from the aorta and the vein occluded just before joining the splenic vein to form the portal vein. Thus, there were 3 groups of dogs—1 in which the superior mesenteric artery alone was occluded, another with the vein occluded, and 1 in which both artery and vein were clamped. In this latter group, the artery was occluded first, and then the clamp was immediately applied

to the vein. The appearance of the bowel was noted at intervals while the clamp was in place, and for a short time after removing it. The superior mesenteric artery was occluded for 1, 2, 3, and 4 hour intervals. The same was true for the vein, and artery and vein together. Four dogs were used for each time interval and the mortality noted. By studying the mortality of occlusion of each vessel or combination of vessels, the time of safe occlusion was obtained. Death in the case of occlusion of the artery was due to peritonitis and general toxemia. In a similar group of animals with arterial occlusion, Sulfasuxidine (0.5 Gm. per kilogram per day in divided doses) was given orally for 7 days preoperatively and continued for 2 days postoperatively. In another group streptomycin (0.5 Gm. twice a day intramuscularly) was administered for 5 days preoperatively and 2 days postoperatively. Since the venous occlusion animals died within a few hours of shock, it was felt that antibacterial agents would be ineffective, and hence these drugs were tried only in the arterial group.

In order to test the role of intravascular clotting under these circumstances, heparin in Pitkin's menstruum was administered to some dogs preoperatively. The use of the drug in this retarding medium has been fully discussed by Loewe and Rosenblatt,[10] and again by Weiner and Lange[18] and will not be elaborated upon here. It is available with or without ephedrine, the use of which results in slower release and prolonged action of the drug. We used the preparation without ephedrine in order to minimize vasospasm of the mesenteric vessels, since Laufman[8, 9] demonstrated that even after the release of arterial or venous occlusion, there is a period of residual vasospasm which causes a continued interference with the intestinal blood supply. The drug was given in doses of 3 mg. per pound of body weight and was administered 2 hours preoperatively. During this time the clotting time rose from a normal level of 5 to 10 minutes to a level of 25 to 50 minutes. At this time the dogs were operated upon and either the superior mesenteric artery or vein was occluded. The clotting time was maintained at an elevated level for 2 days postoperatively by 1 or 2 more injections of heparin. Hemostasis during the operation was rather difficult in some cases, but there were no deaths from hemorrhage.

RESULTS

Arterial Occlusion.—Uniformly, after occlusion of the superior mesenteric artery, the entire small intestine assumes a pale, contracted, rippled appearance. By the end of 1 hour, the color becomes faintly cyanotic; at 2 hours the bowel is relaxed, faintly purplish in color, and responds poorly to stimulation. From this time on, the intestine gradually becomes distended, thin walled, and has a dull pink, lusterless appearance. On release of the clamp there is an immediate hyperemia of the intestinal wall. It becomes bright pink in color, and pulsations are seen in the mesentery (usually feeble if occlusion has been too long).

When death occurred in these animals with arterial occlusion, it was within 12 to 20 hours after the artery was clamped. The bowel was distended, thin walled, and the color mottled, ranging from dull gray to greenish or purple in places. There was usually a small amount of foul-smelling peritoneal fluid.

TABLE I. OCCLUSION OF THE SUPERIOR MESENTERIC ARTERY

DURATION OF OCCLUSION (HOURS)	NUMBER OF ANIMALS	DIED	SURVIVED
½	2	0	2
1	3	1	0
2	4	0	4
3	4	1	3
4	4	3	1

Microscopic section of the bowel revealed degeneration of the mucosa and necrosis of the muscular layers. The cause of death was believed to be due to toxemia and peritonitis which followed when the artery was occluded too long to permit continued intestinal viability.

When the artery was occluded for 2 hours, there were no deaths; for 3 hours the mortality was 25 per cent, and when the vessel was clamped for 4 hours 75 per cent of the animals died (Table I). Apparently in a dog the superior mesenteric artery can be safely occluded for 2 hours. Using Sulfasuxidine to reduce the bacterial flora, the mortality after 4 hours of arterial occlusion was reduced from 75 per cent to 25 per cent (Table II). When the artery was clamped for 5 hours, 66 per cent of the dogs died. In the case of streptomycin, the mortality of 4 hour occlusion was again reduced to 25 per cent, while that for 5 hour occlusion was 50 per cent. There appears to be a definite, but not striking, extension of survival time when the bacterial flora is substantially reduced at the time of arterial occlusion. The use of heparin preoperatively also resulted in a definite extension of the time during which the superior mesenteric artery could be safely clamped (Table IV). When the artery was occluded for 4 hours, the mortality was 25 per cent compared to 75 per cent for the controls. In the 5 hour group, the mortality was still 25 per cent, while when the vessel was clamped for 6 hours, 66 per cent of the animals died.

TABLE II. EFFECTS OF SULFASUXIDINE AND STREPTOMYCIN ON SURVIVAL AFTER SUPERIOR MESENTERIC ARTERIAL OCCLUSION

ARTERIAL OCCLUSION (HOURS)	NUMBER OF DOGS	DIED	SURVIVED
Sulfasuxidine (0.5 Gm. per kg. per day for 7 days preoperatively)			
4	4	1	3
5	3	2	1
Streptomycin (0.5 Gm. twice daily intramuscularly)			
4	4	1	3
5	4	2	2

Venous Occlusion.—Immediately after a clamp is applied to the superior mesenteric vein, the entire small intestine becomes faintly purple in color, and the mesenteric veins are distended with blood. The arteries are constricted and remain so for a time even after release of the obstruction to venous return. With continued venous occlusion, the wall of the bowel becomes darker in color and thicker. Hemorrhages and edema appear in the mesentery. At 2 hours, the intestinal wall and mesentery are considerably engorged, thickened, and

reddish-purple in color. By 3 hours, bloody peritoneal fluid is accumulating, and there is similar fluid in the lumen of the engorged bowel. The wall of the bowel is greatly thickened with blood. The animal is in deep shock due to pooling of a large portion of the blood volume in the mesenteric vascular bed. Death in all cases occurred within 4 hours after the vein was clamped and was due to irreversible shock.

Table III shows the survivals after venous occlusion. In this series there were no deaths when the superior mesenteric vein was clamped for 2 hours, 50 per cent mortality for 3 hour occlusion, and 100 per cent mortality when the vessel was occluded for 4 hours. In the case of 4 hour occlusion, all animals died either a few minutes before the clamp was removed or within 15 minutes afterward.

TABLE III. OCCLUSION OF SUPERIOR MESENTERIC VEIN

DURATION OF OCCLUSION (HOURS)	NUMBER OF ANIMALS	DIED	SURVIVED
1	2	0	2
2	4	0	4
3	4	2	2
4	4	4	0

The use of heparin preoperatively effected a striking change when the superior mesenteric vein was occluded (Table IV). There were no deaths in the 3 and 4 hour groups compared to a mortality for the same group without heparin of 50 per cent and 100 per cent respectively. Furthermore, there were no deaths when the vein was clamped as long as 6 hours. The appearance of the bowel after occlusion of the vein in a heparinized animal was strikingly different from that of the controls. Instead of becoming deep purple and tremendously thickened and engorged with blood, the only change noted was a faintly cyanotic color of the bowel wall. There were only a few tiny hemorrhages in the mesentery, and no bloody fluid was found in the peritoneal cavity or bowel lumen. The collateral channels had apparently completely taken the load from the obstructed superior mesenteric vein.

After this effect of heparin was observed the experiment was carried a step further, and the superior mesenteric vein was ligated in a group of heparinized dogs. The results were even more spectacular. Only 2 of 8 dogs in which the vein was ligated died. The rest recovered quickly from the surgery and showed

TABLE IV. EFFECTS OF HEPARIN ON SUPERIOR MESENTERIC ARTERIAL AND VENOUS OCCLUSION

DURATION OF OCCLUSION (HOURS)	NUMBER OF ANIMALS	DIED	SURVIVED
Venous 3	3	0	3
4	3	0	3
5	3	0	3
6	3	0	3
Vein ligated	8	2	6
Arterial 4	4	1	3
5	4	1	3
6	3	2	1

no ill effects. Two of these dogs were re-explored several weeks later, at which time the intestine appeared entirely normal, and the superior mesenteric vein was still completely occluded.

Arterial and Venous Occlusion.—When both the superior mesenteric artery and vein are occluded, it might be expected that the results would be similar to arterial occlusion alone. This was largely true with certain exceptions. In 2 of the 12 dogs (Table V) in which this procedure was followed, the bowel, before removal of the clamps, presented a picture of venous instead of arterial infarction. This occurred despite the fact that the artery had been carefully clamped and the bowel and mesentery presented a typical picture of arterial occlusion at the time the vein was clamped. Apparently there was some collateral arterial circulation in these dogs allowing some blood to get into the mesenteric circuit. In this group of combined occlusion the mortality was 25 per cent for the 2 hour group, 25 per cent for the 3 hour group, and 50 per cent when the vessels were clamped for 4 hours.

TABLE V. OCCLUSION OF THE SUPERIOR MESENTERIC ARTERY AND VEIN

DURATION OF OCCLUSION (HOURS)	NUMBER OF ANIMALS	DIED	SURVIVED
2	4	1	3
3	4	1	3
4	4	2	4

DISCUSSION

Some objections may be voiced to applying such results directly to human surgery. Noer[13] has pointed out important differences between the intestinal circulation of man and the common laboratory animals. Anastomoses between vasa recta, a plexus of vessels along the mesenteric border, and surprisingly adequate intramural anastomoses give the intestine of the dog a greater revascularizing potentiality. This, however, applies chiefly to interruption of vascular supply to a segment of bowel, in which case anastomoses with vessels of the adjoining segments permit revascularization if the devascularized segment is short. When the arterial or venous supply to the entire small intestine is interrupted, however, collateral channels within the mesentery and bowel itself can hardly be sufficient to supply the bowel. Under these circumstances, however, the only differences between the dog and human intestine would be differences in the collateral circulation of the small intestine as a whole.

That potential, but probably immediately inadequate, collateral channels of circulation to the midgut exist is evidenced by the reports of Blalock and Levy,[1] Laufman,[7] and Brunschwig.[2] Among these avenues are anastomoses (1) between the celiac and superior mesenteric axis via the pancreaticoduodenal vessels, (2) with the inferior mesenteric vessels and thence to the systemic circulation through the hemorrhoidal plexus, (3) with the retroperitoneal and lumbar and azygos vessels, and (4) through the omentum and abdominal wall. Also, venous inosculations with the renal veins have been described.[16] Since

these collaterals are ineffective after sudden occlusion of the superior mesenteric vein but can be made effective by heparinization, it would appear that thrombosis or a prethrombotic phenomenon such as "sludging" with a retarded flow prevents these potential channels from operating effectively immediately. Our findings are contrary to the report of Laufman,[6] who observed that heparinization in the presence of 3 hour strangulation of loops of small bowel was associated with increased bleeding into the infarcted area and resulted in death of 8 out of 9 animals. However, in the experiments reported by Laufman it is possible that once thrombosis is established, as it apparently was in his animals, heparinization was ineffective in altering the situation and was conducive to increased bleeding. Also, since the entire loop was strangulated by a tape there was no possibility of collateral venous channels draining off the pooled blood. In our experiments, on the other hand, where the main venous avenue alone was occluded, by preventing thrombosis and vascular damage from occurring, heparinization maintained patency of collateral channels, and no bleeding into the potentially infarcted area occurred.

It seems apparent that if anticoagulant therapy is in effect at the time of venous occlusion, thrombosis is prevented and the collateral channels are able more adequately to take over the load. Support of this concept is found in a case reported by Schnug[16] in 1943. The patient had suffered an abdominal gunshot wound, and on exploration it was discovered that a large hole had been torn in the superior mesenteric vein. The defect could not be repaired so the vein was ligated. The patient was heparinized immediately, and the clotting time maintained at elevated levels for 5 days. Reoperation showed a fairly normal bowel.

The effects of heparin on arterial occlusion were not nearly as striking as those on venous occlusion but did significantly extend the period during which occlusion could be tolerated. This suggests that here also some improvement in collateral flow may have resulted. It is also possible that thrombosis, as a result of stasis, was prevented in the capillaries so that when arterial inflow was again permitted, circulation through the gut could be more effectively maintained.

The antibacterial agents streptomycin and Sulfasuxidine, by retarding bacterial proliferation, improved slightly the survivals after arterial occlusion, probably by delaying bacterial penetration into the gut while its viability was impaired as a result of ischemia.

SUMMARY

1. The effects of occlusion of the superior mesenteric artery and vein have been discussed.

2. The cause of death from arterial occlusion is peritonitis and occurs from 12 to 20 hours after the vessel is clamped. When the superior mesenteric vein is occluded, death occurs within 4 hours from shock.

3. Either the superior mesenteric artery or vein can be safely occluded for 2 hours. Continued interruption is dangerous.

4. The use of Sulfasuxidine or streptomycin to reduce the intestinal bacterial flora before surgery somewhat extends the time of safe occlusion.

5. Heparin administered preoperatively to prevent intravascular clotting produced extension of the time of safe occlusion. It is particularly effective in the case of venous occlusion.

6. The superior mesenteric vein was ligated in 8 heparinized dogs and 6 animals survived.

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PORTAL VENOGRAPHY

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EXTENSIVE resections of liver tissue have recently been performed at the University of Minnesota Hospitals in cases of metastatic carcinoma of the liver. The frequency of these liver resections provided the impetus for the present study of the contrast roentgen visualization of the portal vein and the intrahepatic portal vein radicals. This procedure has been given the descriptive term of portal venography. Thus far the work has been concerned primarily with the technical factors. Practical applications of portal venography remain to be determined.

Literature pertinent to portal venography is extremely meager. No direct reference to this subject has as yet been found. Farinas,[1] in his paper on abdominal venography stated, that Diodrast injected into the saphenous vein in cases of anastomosis of the trunks of the inferior vena cava and portal vein shows the venous circulation of both trunks. Farinas' paper includes a roentgenogram illustrating good contrast filling of the inferior vena cava, the portal vein, and the portal radicals within the liver. Blakemore[2] has used venography at operation to demonstrate the site of extrahepatic portal obstruction. He has injected Diodrast into the coronary vein and is of the opinion that the procedure is not only of value in determining the site of portal block but also of confirming the site of junction of the coronary vein with the larger portal trunks.

The portal venographic examinations done thus far at the University of Minnesota Hospitals have been performed as an incidental procedure in the operating room on patients undergoing various surgical procedures requiring laparotomy. The technique consists of first inserting a Polythene catheter (I.D. 066, O.D. 095) into one of the tributaries of the portal vein. The right gastroepiploic vein has most often been used. After insertion, the catheter is advanced proximally until the tip is in the portal vein. After tying the catheter in place, 20 c.c. of 35 per cent Diodrast are injected through the catheter as rapidly as possible. Preferably the injection should be completed in two or three seconds. Immediately upon completion of the injection a radiographic exposure is made. The radiographic work has been done with a mobile 50 M. A. x-ray machine and a hand-operated Potter-Bucky diaphragm.

With the technique described, satisfactory roentgenograms of the portal vein and radicals have been obtained with a fair degree of consistency. Figs.

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1 and 2 demonstrate the result that may be expected with this technique. In most instances 35 per cent Diodrast has been used and found satisfactory for this type of visualization, although a limited number of portal venograms have also been made using 70 per cent Diodrast. Fig. 3 is an example of a portal venogram made with the 70 per cent solution. Better contrast and more complete filling can be expected with the more concentrated contrast material, but 70 per cent Diodrast has not been used routinely because of the possibility of serious reactions. On the other hand, in addition to the portal visualization, opacification of the entire liver may be desirable; such opacification necessitates the

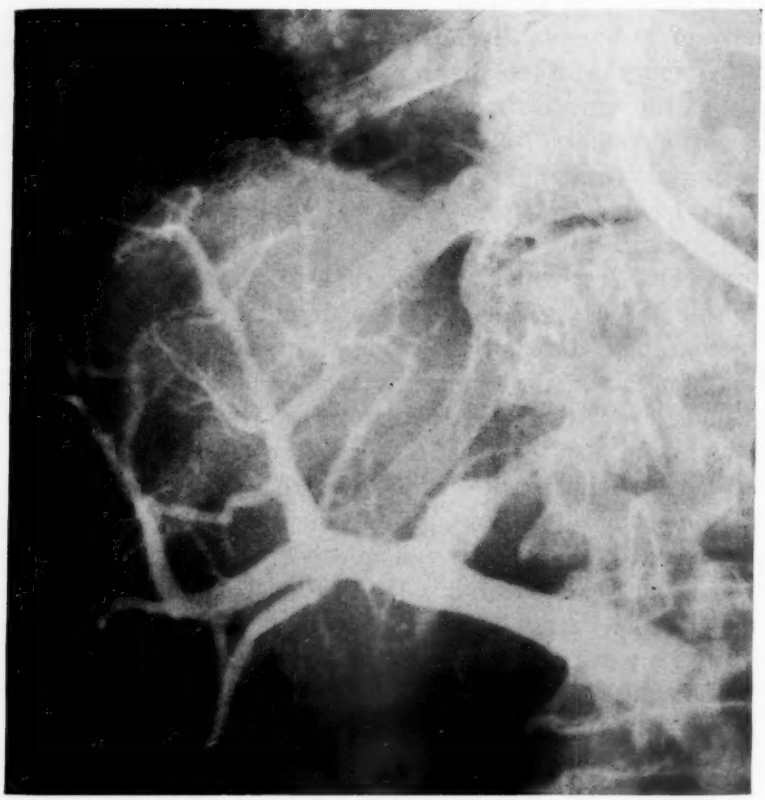

Fig. 1.—Portal venography with 35 per cent Diodrast. Incomplete filling of left branch of portal vein.

use of 70 per cent Diodrast. Also, in order to visualize the liver as whole, the timing of the radiographic exposure must be such as to permit the contrast material to reach the liver sinusoids. Fig. 4 demonstrates fairly good opacification of the liver with 70 per cent Diodrast. The density of 35 per cent Diodrast is not sufficient to produce this type of roentgenogram. It must be pointed out in this regard that if an attempt is made to visualize the portal radicals and also to opacify the liver, two separate injections must be made along with concomitant radiographic exposures. The use of a rapid cassette changer to permit multiple serial roentgenograms would be highly desirable. Serial roentgeno-

grams would obviate the necessity for two separate injections and would in all probability provide more consistent results. However, no practical equipment of this type that can be adapted to the operating room is available at present.

There have been no serious reactions or complications resulting from portal venography. In one instance a decrease of 30 mm. in the systolic blood pressure occurred shortly after the injection. This phenomenon, however, was transitory. On two occasions there was extravasation of the contrast medium but no sequelae of any consequence resulted. Extravasation may occur if the tip of the Polythene catheter is not in the portal vein; with the tip of the catheter properly placed this complication is eliminated.

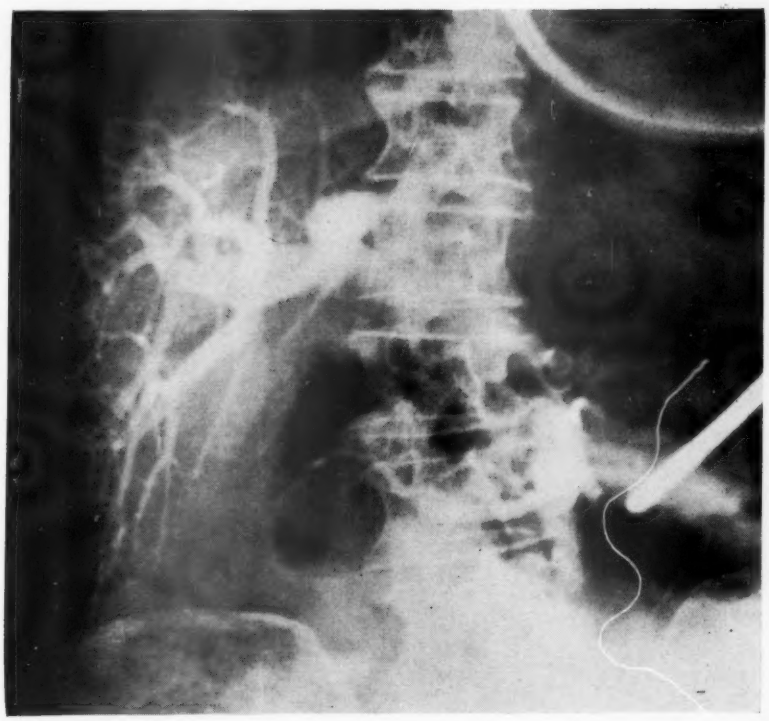

Fig. 2.—Portal venography with 35 per cent Diodrast. Incomplete filling of left branch of portal vein. Note retrograde filling of portal tributary veins.

Most of the unsatisfactory examinations were the result either of failure to pass the tip of the catheter into the portal vein or failure to inject the contrast medium into the circulation with sufficient rapidity. In the former instance the dye was often dissipated into the tributary portal channels or extravasation occurred as a result of the force of the injection. When the contrast medium was not injected with sufficient rapidity, excessive dilution of the medium in the blood stream resulted in faint visualization or nonvisualization of the portal radicals. Several otherwise satisfactory venograms were lacking in fine detail because of the occasional difficulty in controlling respiration at the time of radiographic exposure. Also a few unsatisfactory examinations

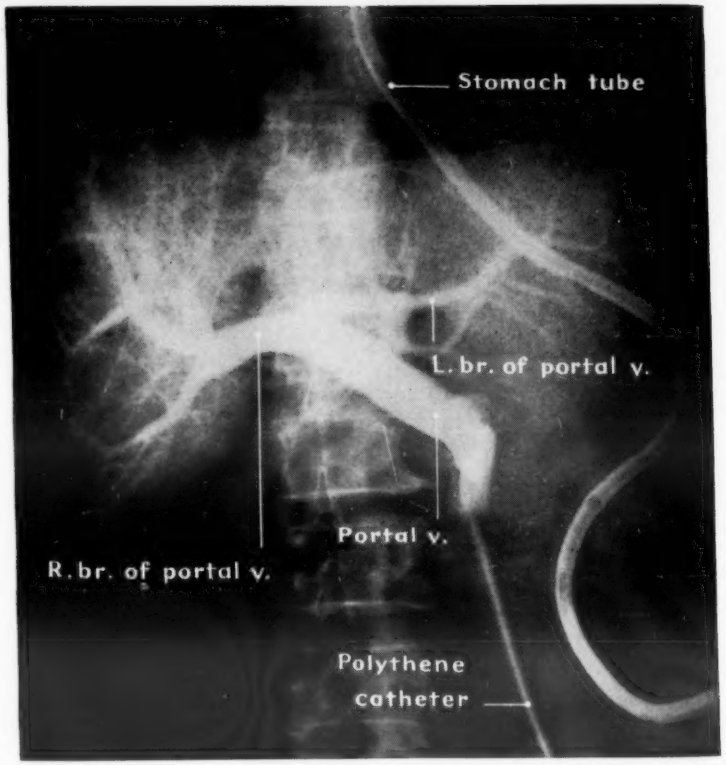

Fig. 3.

Fig. 4.

Fig. 3.—Portal venography with 70 per cent Diodrast. Complete filling of left branch of portal vein. Respiration not completely controlled with resultant imperfect detail.

Fig. 4.—Opacification of liver with 70 per cent Diodrast.

were attributable primarily to radiographic technical difficulties attending the use of a relatively low-power x-ray unit in the operating room.

The technical details that favor good visualization of the portal radicals may be summarized as follows:

1. Direct injection of the contrast medium into the portal vein.
2. Rapid injection of the contrast medium.
3. Complete arrest of respiration during x-ray exposure.
4. Proper timing of the x-ray exposure in relationship to the injection of the contrast medium.

SUMMARY

A method for the roentgen contrast visualization of the portal vein and the portal radicals within the liver is presented. This visualization has been given the descriptive term of portal venography. (No direct reference to this procedure has as yet been found in the literature.) The practical applications of portal venography remain to be determined.

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THE SURGICAL MANAGEMENT OF CHRONIC INDURATED CELLULITIS OF THE LOWER EXTREMITY (THE INDURATED LEG)

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CHRONIC indurated cellulitis refers to the "indurated leg." Usually the induration has occurred as a late sequela of mismanaged iliofemoral thrombophlebitis. Recurring episodes of thrombophlebitis in varicose veins, repeated attacks of lymphangitis-streptogenes, local trauma, may produce the same pathology. It is the inevitable result of lymphedema, whatsoever the cause.

The disease is limited to the lower leg, usually extending from the malleoli to several inches below the knee. The characteristic feature is marked induration of the subcutaneous tissues. The induration is permanent and is present when the patient awakens in the morning, in contrast to lymphedema which recedes overnight. The overlying skin may appear normal, may be pigmented, eczematoid, preulcerous, or ulcerated. Extensive varicosities may exist in the thigh but those present in the lower leg are usually masked by the chronic indurated cellulitis, or have become obliterated by previous thrombosis.

Chronic venous insufficiency, anoxia, fibrosis, dilated and obstructed lymphatics, varicosities, incompetent perforating veins, incompetent deep veins, calcified fat, and thickened deep fascia form a formidable pathologic background. However, no matter how extensive the skin, the subcutaneous tissue, and the fascial damages are, the structures deep to the fascia are invariably normal. The underlying muscles are red, well-vascularized, and nonedematous, and form an excellent bed for resutured skin flaps or for the immediate application of a split-thickness skin graft.

Conservative therapy has little to offer in chronic indurated cellulitis. A saphenous ligation, a femoral ligation, or both cannot be expected to change the irreversible pathology in the lower leg. The induration, the discomfort are the patient's for life unless the problem is radically approached. It is also futile to excise locally indolent ulcers in these cases. Recurrence is inevitable in subsequent years unless the surrounding diseased tissue is resected and the pathologic venous circulatory state corrected. A period of bed rest and leg elevation may tide over an attack of dermatitis or cellulitis, or heal an early ulcer. Unna paste boots or elastoplast bandages, worn for many weeks, may temporarily reduce the leg swelling and add comfort to the patient. Large indolent ulcers may even be made to heal. But the results of conservative therapy are about as temporary as painting is over bad plaster. Healing has occurred by scar formation over a bed of fibrosed tissue, inadequate in venous,

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arterial, and lymphatic circulation. A slight trauma, the recurrence of dependent edema, or merely a return to normal ambulation are sufficient to cause the skin to break down again.

The surgical management of chronic indurated cellulitis consists essentially of removing widely all of the abnormal structures of the involved area—always the subcutaneous tissue and fascia, and when devitalized or ulcerated, the overlying skin—and covering the defect with skin resting on well-vascularized muscles. Existing venous pathology is corrected simultaneously. If the saphenous vein is varicosed, it is ligated high and removed by stripping; if the femoral vein is damaged and incompetent, a superficial femoral or popliteal vein ligation is performed or even the femoral vein resected; if both saphenous and femoral systems are damaged, a high saphenous ligation and a superficial femoral ligation are simultaneously performed.

SURGICAL TECHNIQUE FOR CHRONIC INDURATED CELLULITIS WITH RELATIVELY NORMAL OVERLYING SKIN

1. Low spinal pontocaine glucose or intravenous Pentothal Sodium is used for anesthesia. The extremity is prepared with the foot free, wrapped in a sterile towel so that the ankle region is exposed. A sterile sheet is placed under the affected leg and over the opposite leg and the draping is finished. The extent of the induration is determined by palpation. The patient is placed in Trendelenburg position and the leg further elevated by placing the heel in an upturned basin. This is important as it greatly reduces the loss of blood during the first phase of the operation.

2. A longitudinal skin incision is made from the lower to the upper limits of the induration and passing through its center. This usually involves an incision from the region of the internal malleolus to a point several inches below the knee and midway between the anterior and posterior border of the leg. The lower limit of the incision should pass posterior to the internal malleolus, rather than over it (Fig. 1, *1*).

3. The upper limit of the incision is rapidly deepened through the subcutaneous tissue and the fascia, exposing the underlying muscle. Two fingers are inserted into the subfascial space and the subcutaneous tissue and fascia are cut open for the entire length of the skin incision (Fig. 1, *2*).

4. The full-thickness flaps of skin, subcutaneous tissue, and fascia are now readily stripped back bluntly to the tibial crest anteriorly and the midleg posteriorly. Bleeding is controlled by covering the flaps with gauze and applying manual compression. As the anterior flap is turned out, a number of perforating veins, usually incompetent perforators, is seen passing from an anterior branch of the saphenous vein through the fascia into the deep veins along the border of the tibia. These perforators are individually clamped, divided, ligated (Fig. 1, *3* and Fig. 2, *4*).

5. The flaps are turned out and the fascia incised, from within out, and beyond the limits of the induration for the whole length of each flap. Delineation of the deep tissue to be removed is finished by dividing the fascia at the upper and lower end of the incision (Fig. 2, *5*).

6. The anterior and posterior flaps are pared of all fascia and subcutaneous tissue. A series of towel clamps grasp the skin edges and Ochsner clamps grasp the fascia. These clamps are used to apply traction and to separate the tissues, as, by a process of opening, closing, and cutting with the dissecting scissors, the entire previously delineated segments of pathologic tissue are re-

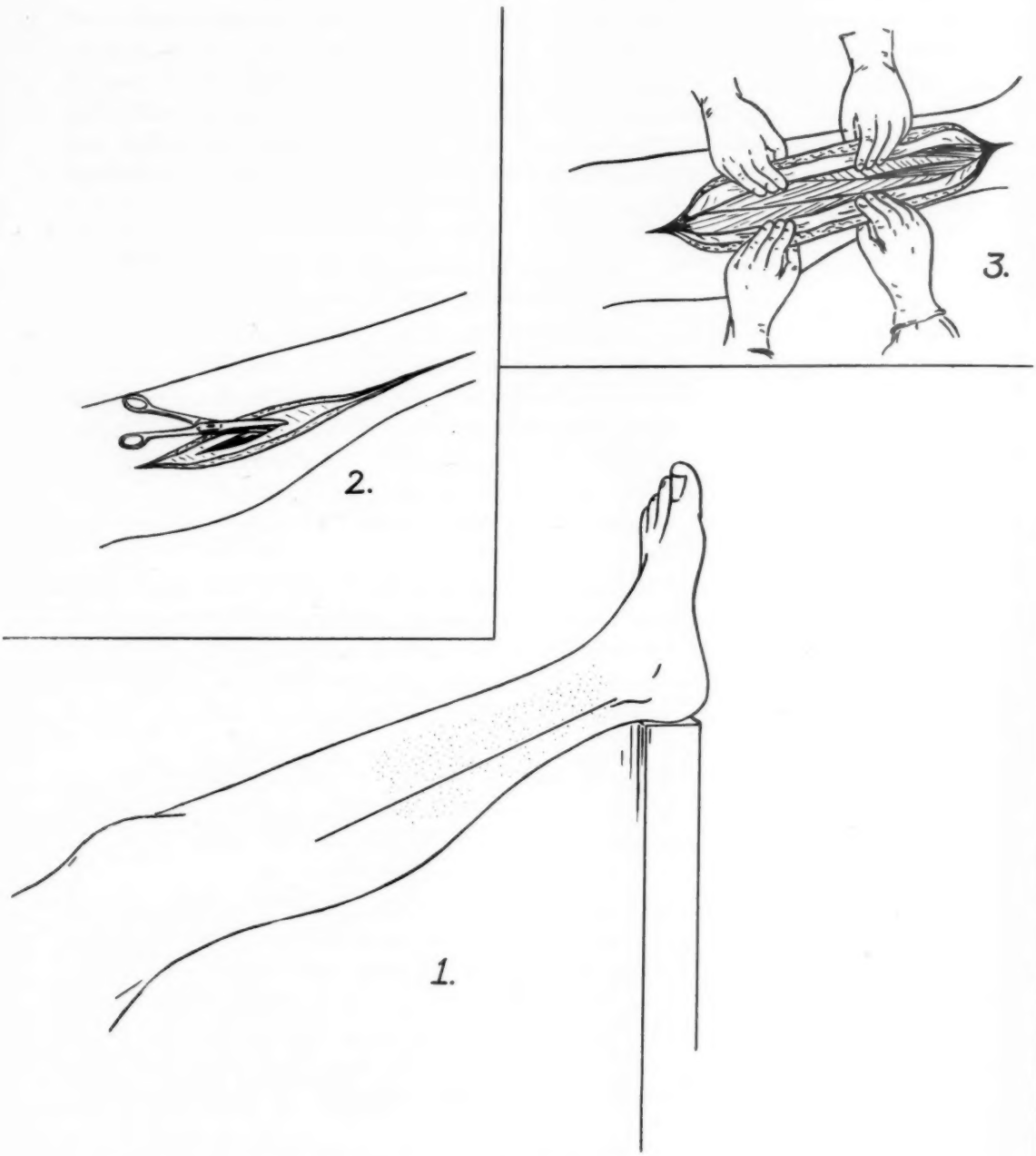


Fig. 1.—The indurated leg operation. *1*, Patient is in Trendelenburg position, foot elevated, incision through center of the area of induration. *2*, Upper end of incision deepened through fascia, and fascia and overlying tissue split open the entire side of the leg. *3*, Flaps dissected back and bleeding controlled with manual compression. Muscles exposed.

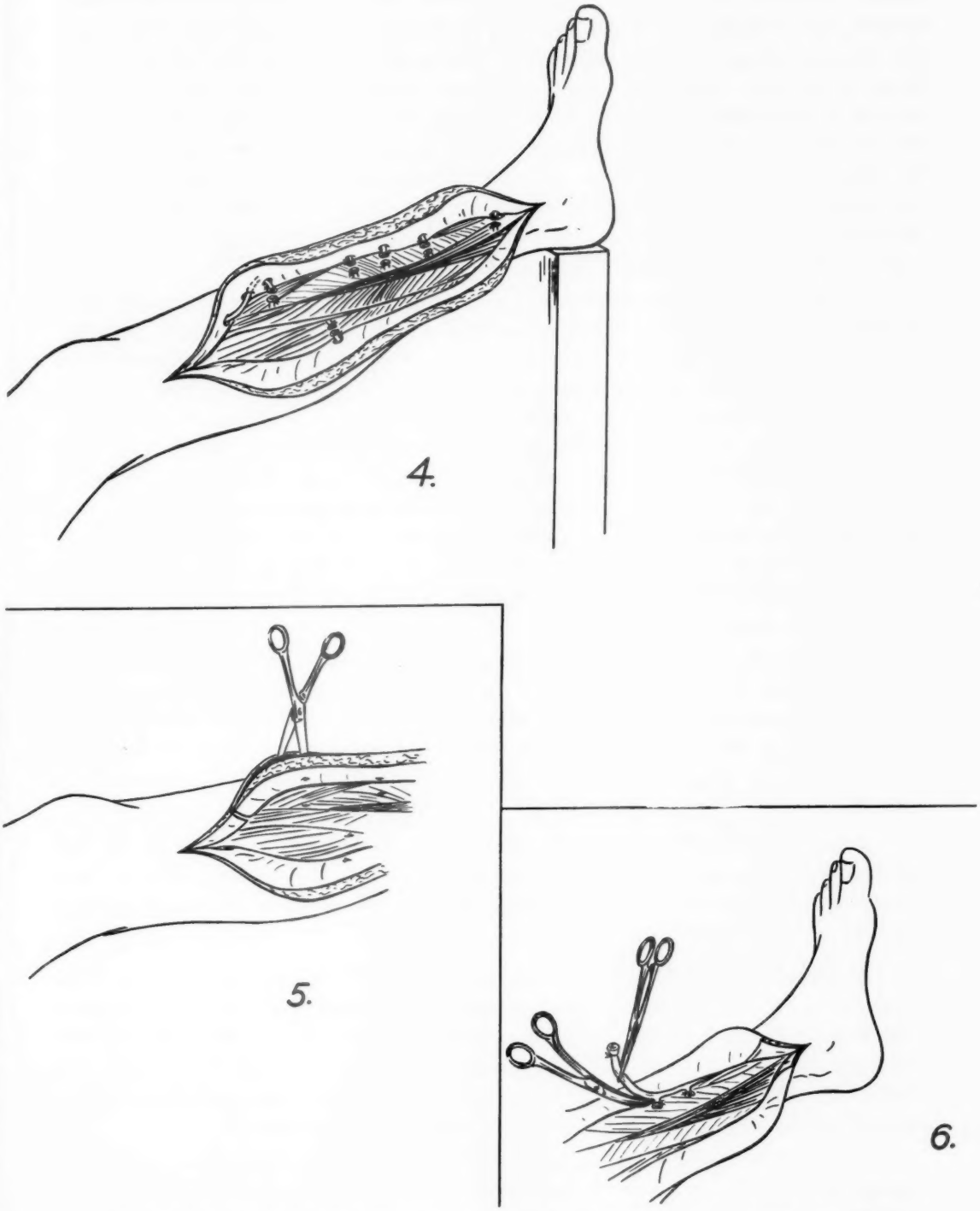


Fig. 2.—The indurated leg operation. *4*, Incompetent perforating vein in the angles of the flaps divided and ligated. Long saphenous vein is indicated in the subcutaneous fat of the anterior flap passing up into the thigh. *5*, The indurated subcutaneous tissue and fascia are resected from each flap, leaving only skin flaps and exposed healthy muscle. *6*, The main branch of the saphenous vein is excised from the angle of the anterior flap.

moved. The line of cleavage is just within the skin edge, but hard work, sharp scissors, and a strong hand are required to dissect off the indurated, even calcified, fat and fascia. The saphenous vein will usually be encountered at the upper limits of anterior dissection and is clamped, divided, ligated. After the dissection is completed, the distal portion of this vein is seen in the angle between the anterior flap and the tibial border. It is again divided and ligated above the ankle and entirely resected. The hemostasis is completed. Larger bleeders are clamped and ligated. Usually there are a number of oozing points that are difficult to clamp. These are best coagulated with the Bovie apparatus, using sharp-pointed bayonet forcep (Fig. 2, *6*).

7. The skin flaps are inspected for viability. The edges are trimmed back to well-vascularized skin. There is usually more skin than is needed and the excision of a few millimeters from each flap prevents necrosis of the subsequent suture line. One or two stab wounds are made in the posterior flap through which Penrose tissue wicks are inserted for drainage. The skin flaps are approximated with interrupted sutures of silk. Should some tension be present, the flaps are pie-crusted with jabs of a No. 15 Bard-Parker blade. Should undue tension exist, no attempt is made to close the wound completely. Instead, the skin edges are tacked to the underlying muscle and the defect covered immediately with a split-thickness skin graft, as described later in this paper. The dressing consists of a thick roll of gauze from foot to knee and a 4 inch wide, No. 8 Ace bandage (Fig. 3, *7* and *8*).

The Penrose tissue drains are removed in 48 hours. The patient may be ambulatory on the seventh day but the stitches are usually left in until the tenth or eleventh day because of the slow rate of healing of the undermined flaps. The patient is required to wear the elastic leg bandage until all tendency to leg swelling has disappeared, often for a period of several months (Fig. 4, *A* and *B*).

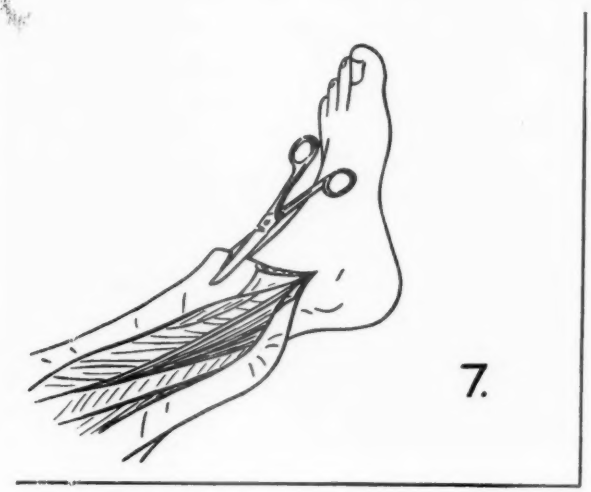
When induration is present in both the inner and outer aspects of the leg, an identical operation is performed on the outer side of the leg about 10 days later. The sural nerve should be identified and preserved when this dissection extends to the midline posteriorly.

Modification A: Surgical Technique for Chronic Indurated Cellulitis With Pathologic Overlying Skin.—The surgical management of chronic indurated cellulitis requires the removal of all abnormal tissue. When the overlying skin presents the scars of healed ulcers, the pigmentation or bluish discoloration of venous stasis, the weeping or scaling of dermatitis, it should be sacrificed and a split-thickness graft used to resurface the underlying muscles.

1. The skin incision begins above the upper level of induration and passes downward to encircle the devitalized skin area. The patient is in Trendelenburg position and the leg is elevated.

2. The upper limit of the incision is deepened through the subcutaneous tissue and fascia, exposing the muscles. Two fingers are inserted into the subfascial space and the subcutaneous tissue and fascia are cut open down to the

devitalized skin area, previously outlined by the skin incision. With the fingers still between muscle and fascia, this area is freed bluntly and the skin, indurated underlying tissue, and fascia are excised en bloc.



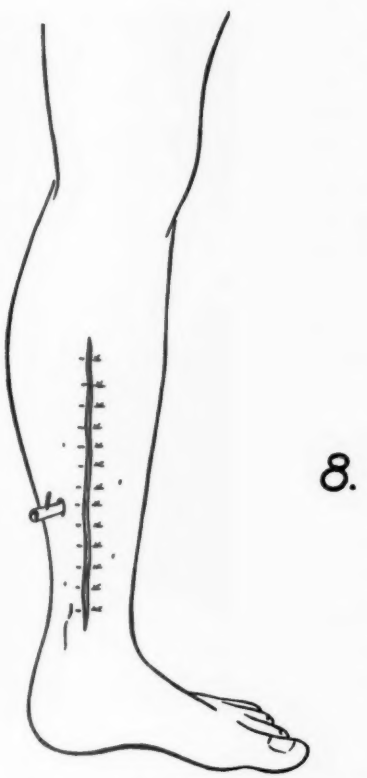


Fig. 3.—The indurated leg operation. 7, Excess and devitalized skin is excised from each skin flap to prevent necrosis of the suture line. 8, Skin flaps closed over muscles with interrupted silk sutures. Penrose drain through a stab wound.

A.

B.

Fig. 4, *A* and *B*.—Typical uncomplicated postthrombophlebitic chronic indurated cellulitis. An incision was made over the indurated area, and all tissues between the skin and muscles were resected after the manner described in the text. *A*, preoperative; *B*, postoperative.

3. The anterior and posterior flaps are pared of all fascia and subcutaneous tissue as described in the previous section. Extensive undermining of the flaps at the area of skin excision is avoided as this interferes with successful grafting of the area.

4. The upper end of the incision is closed with interrupted silk stitches. The skin edges are tacked about the excised area to the underlying muscles with mattress sutures placed several millimeters back from and parallel to the skin edges. This narrows the defect and furnishes a continuous free skin border to which the skin graft may be sutured.

5. A split-thickness graft is obtained from the thigh, using the Padgett dermatone set at .016 inch. While preparations are being made for the graft, an assistant elevates the leg even higher. This maneuver plus previous hemostasis will usually result in a dry recipient area.

6. The graft is transferred to the recipient area, using towel clips to clip it to the skin edges at numerous points. This immediately fixes the graft to its future bed, so that it can be cut to pattern and sutured wihout motion. Excess graft is excised, but the pattern should overlap the border of the defect by several millimeters.

7. Continuous fine silk or silver wire is used to suture the graft in place. This suture passes through the graft from without in and then through the skin edge from within out piling the few millimeters of excess graft onto the free skin edge. Passing the needle into the skin border first would result in elevating the graft from its bed as each stitch is placed, an undesirable feature. The graft is further fixed to the surface of the defect with a few interrupted sutures. The graft is pie-crusted sparsely with a few jabs of a Bard-Parker No. 15 blade.

8. Several cubic centimeters of penicillin solution (500 units of penicillin per cubic centimeter) are injected under the graft, and it is pressed evenly against its bed.

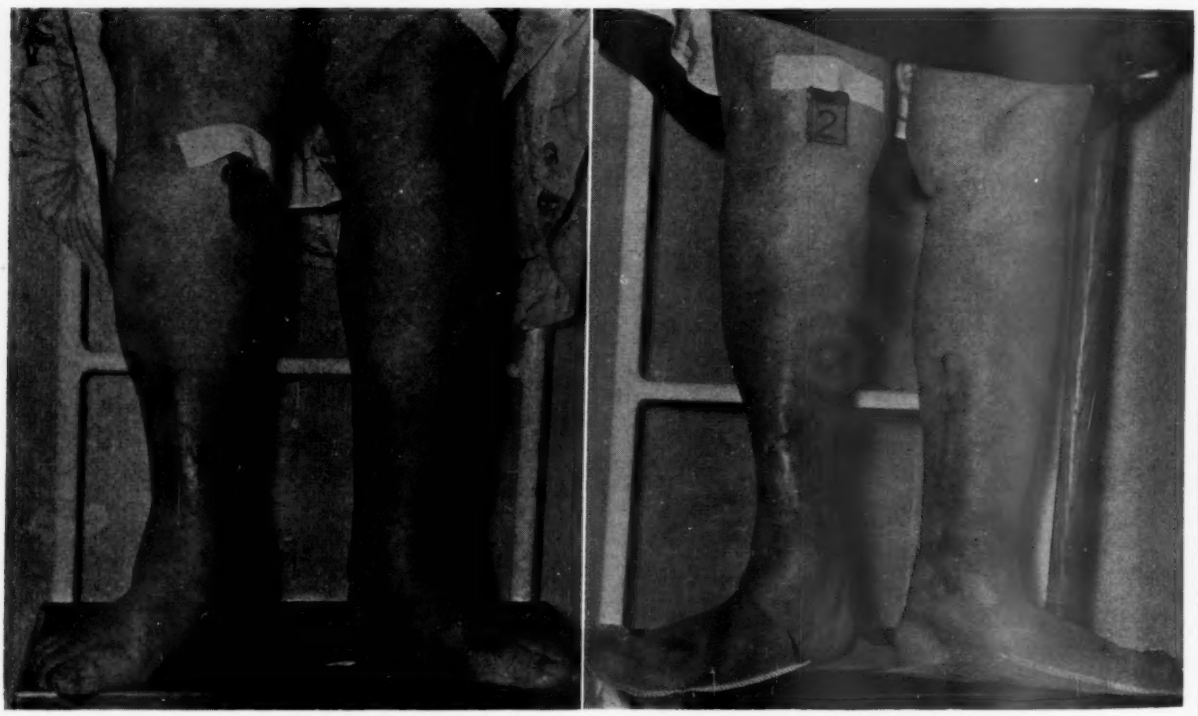
9. The grafted area is dressed with Xeroform gauze, flat gauze moistened in saline solution, and a wide piece of sponge rubber for even pressure. The leg is wrapped from foot to knee with "ripple" gauze followed by a 4 inch No. 8 Ace leg bandage. The leg is placed in a well-padded, foot-to-knee posterior metal splint with foot attachment, and the splint is held in place wth a second Ace bandage. The donor site is dressed with Xeroform gauze and flat gauze.

The first dressing is usually on the seventh or eighth postoperative day. The graft is again covered with Xeroform gauze and flat gauze and the leg wrapped evenly with an Ace No. 8 bandage. The sponge rubber and posterior metal splint are omitted. The stitches may be removed at the first or subsequent dressing. Complete healing is usually present by the fourteenth day (Fig. 5, *A* and *B*).

Pathologic skin changes may exist at sites other than the mesial aspect of the leg above the internal malleolus. It may be necessary to sacrifice skin over the tibial crest, in the calf, or over the lateral as well as the mesial aspect of the leg. In the latter instance it is well to leave a small strip of skin to which

to sew the graft. By staged procedures it is even practical to excise the skin, subcutaneous tissue, and fascia of the entire circumference of the leg (Fig. 6, *A* and *B*).

Modification B: Surgical Technique for Indolent Leg Ulcer and Chronic Indurated Cellulitis.—A preoperative period of hospitalization is usually necessary to rid the ulcer of virulent bacteria. The therapy varies, of course, with the local findings. Penicillin parenterally supplemented by penicillin-urethane solution (1,000 units of penicillin per cubic centimeter in a ½ per cent urethane saline solution) or tyrothricin solution (0.5 mg. per cubic centimeter) locally works well. It is not necessary to wait for the ulcer to heal before attacking it surgically, for in the technique herein described the ulcer area is early excluded from the operative field.



A. *B.*

Fig. 5, *A* and *B*.—Bilateral postthrombophlebitic chronic indurated cellulitis. Preulcerous devitalized discolored skin above internal malleolus of right leg. The surgery included bilateral resection of the fibrosed and calcified subcutaneous tissue and fascia. The devitalized skin on the right leg was sacrificed and a split-thickness graft applied. There is no postoperative edema. *A*, preoperative, *B*, postoperative.

1. With the back of the scalpel a circle is marked about the ulcer, defining the local area to be resected. This area is covered with gauze which is sewed or clipped in place so that the ulcer area is no longer seen throughout the operation.

2. The skin incision is begun well above the upper level of the induration and passes downward to encircle, in this instance, the gauze-covered ulcer and surrounding abnormal skin.

3. The subfascial space is entered above the ulcer as described in the previous section and the fingers are used to separate bluntly the fascia and overlying ulcer from the muscles. With a wide sweep of the knife, the ulcer and surrounding skin and the underlying subcutaneous bed and fascia are removed en masse. The important point is the preliminary elevation of the fascia off the muscles, because at the ulcer site the fascia is often adherent to muscle and periosteum. By entering the subfascial space well above the ulcer, the proper line of cleavage between the fascia and muscle is obtained.

A. *B.*

Fig. 6.—*A*, Varicose veins, chronic indurated cellulitis, and chronic dermatitis involving the anterior surface of the leg. Note primary take of the split-thickness graft on muscle and periosteum.

B, Chronic indurated cellulitis and chronic dermatitis. Note the excellent result when the resection is wide, removing all pathologic tissue.

4. The skin flaps are pared of pathologic fat and fascia as described in the previous section and the defect created by removing the ulcer and surrounding skin is covered with a split-thickness skin graft (Fig. 7, *A*, *1*, *2*, *3*).

5. The grafted area is dressed as previously described, but covered with flat gauze moistened in saline solution, and 1 or 2 No. 18 rubber catheters are incorporated in the dressing. During the first postoperative week the dressing

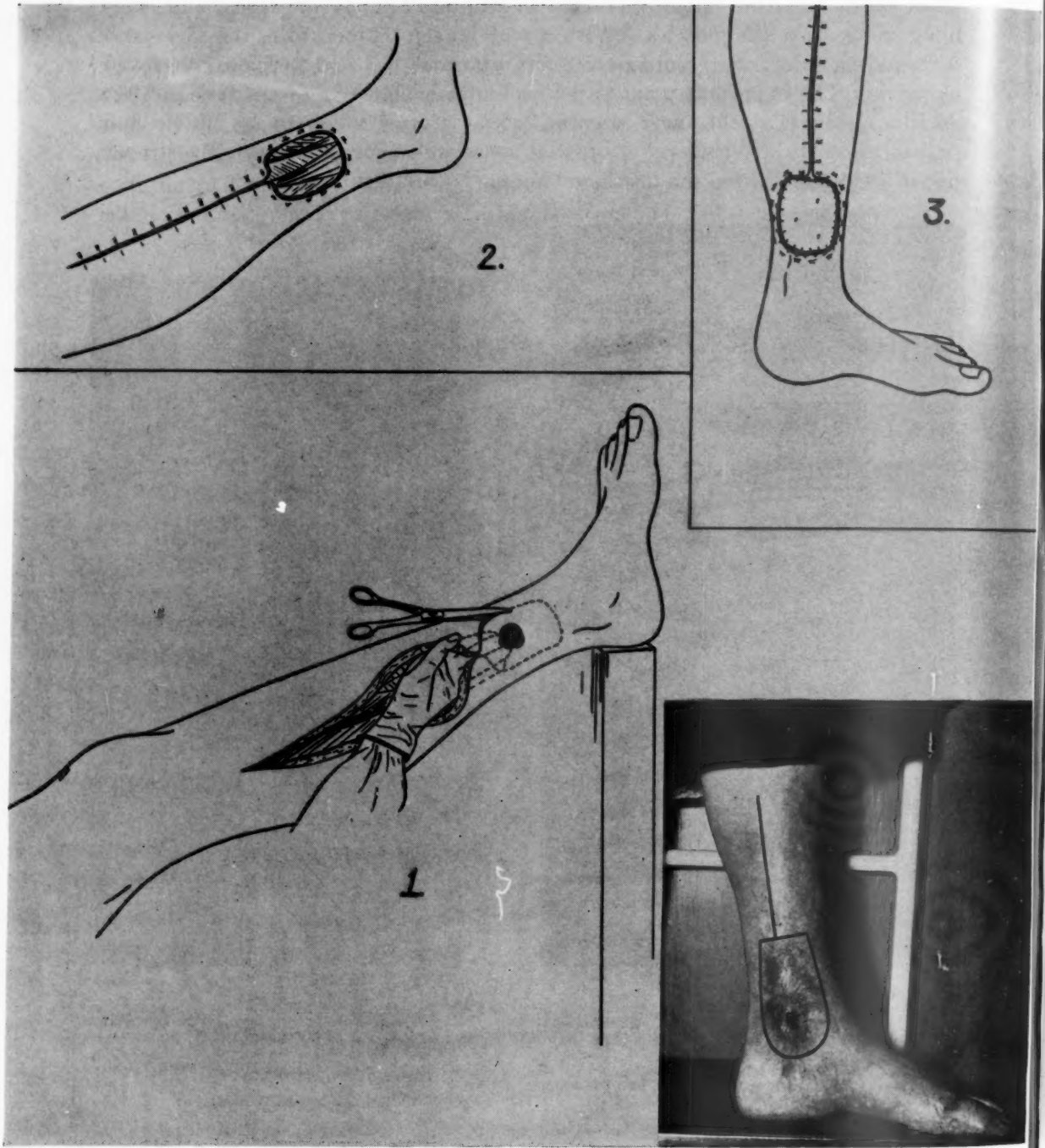
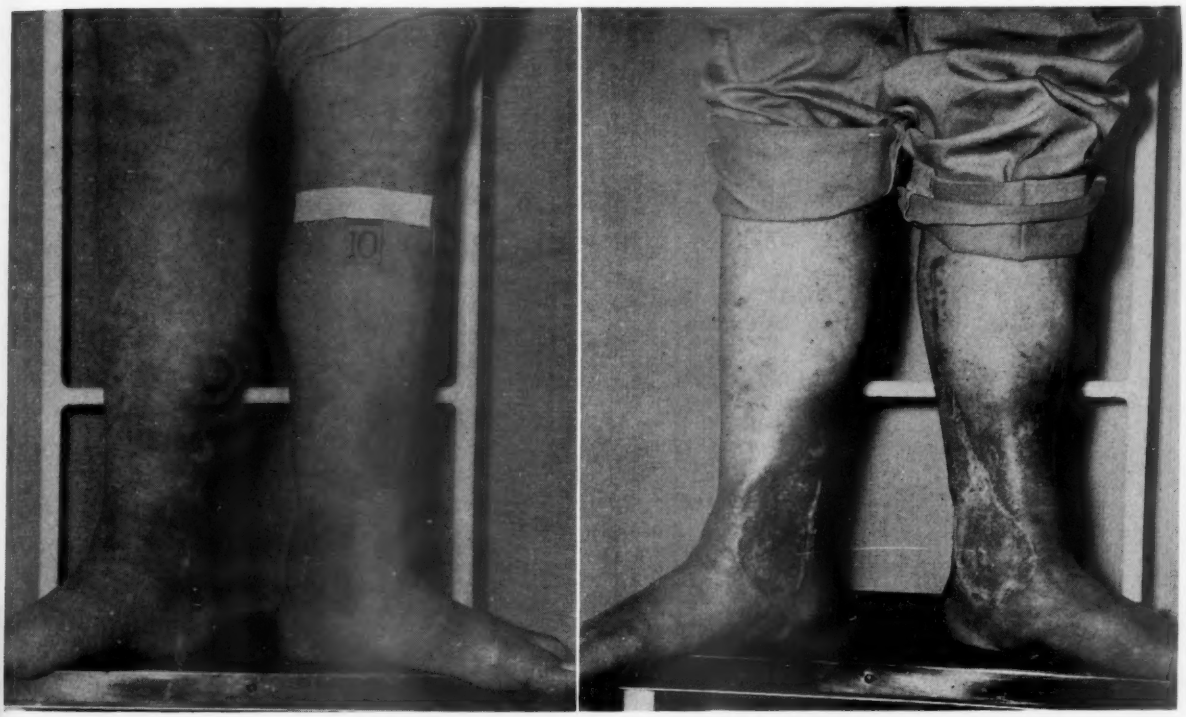


Fig. 7.—The operation for the indurated leg and indolent leg ulcer. *A*, The proposed incision has been traced on the leg as indicated in the figure to the right. *1*, The operation has been begun by making a high subfascial incision. The ulcer is freed bluntly from the underlying muscles and tendons by dissection in the subfascial space. *2*, The upper skin flaps have been pared of fat and fascia and resutured. The ulcer defect has been narrowed by suturing in the skin edges. *3*, The defect has been covered with a split-thickness graft.

is kept wet by injecting glycerine 15 per cent, acetic acid ½ per cent, saline solution through the catheters every 8 hours. The ends of the catheters are brought out of the upper end of the dressing and are kept sterile at all times by covering them with gauze after each injection. By using this wet method of handling the grafted area, the dreaded pyocyaneus infection is avoided and a primary take on these badly infected legs can be accomplished at the first operation (Fig. 8, *A* and *B*; Fig. 9, *A* and *B*).



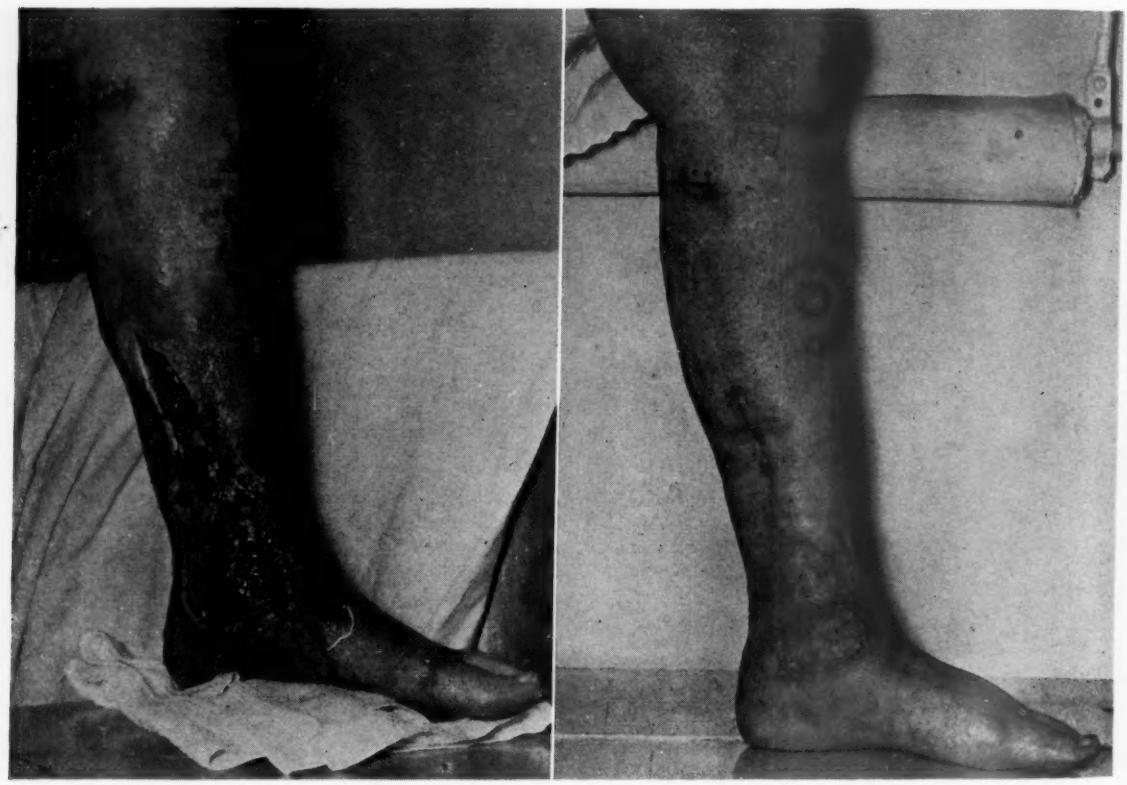
A. *B.*

Fig. 8, *A* and *B*.—Lymphedema developed subsequent to x-ray therapy for seminoma of the testicle. Nine years later the patient presented himself with typical chronic indurated cellulitis and indolent ulcers on the mesial and lateral aspect of both legs. In a one-stage operation the "indurated leg procedure" was performed on the mesial and lateral aspects of both legs and all 4 indolent ulcers excised and grafted. *A*, preoperative; *B*, postoperative.

Modification C: Surgical Technique for Indolent Leg Ulcer, Exposed Bone, and Chronic Indurated Cellulitis.—The surgical management is similar to that described previously for the indurated leg and indolent ulcer. If normal unscarred periosteum presents, it is left intact as far as possible and the split-thickness graft applied to it and the surrounding muscle. The part of the graft overlying the periosteum will usually die. It acts, however, as an excellent covering for the periosteum during the formation of granulation tissue. On the ninth or tenth postoperative day, the dead portion of the graft is excised and a second split-thickness graft applied immediately, usually now with complete success.

When diseased bone is present, the periosteum is stripped just sufficiently to gain access to the diseased area. Commencing at one end, the cortical bone is

cut away layer by layer, until a smooth open surface of normal bone remains. The cortex will now be of split thickness, the outer layer having been sawed away. The soft part and bone defect is then covered with a split-thickness graft. Surprisingly enough, the entire graft will usually take, in spite of the fact that cortical bone forms part of the bed. This is especially so if the bone area is small. Should part of the graft die, a regrafting is done as described previously.



A. *B.*

Fig. 9, *A* and *B*.—A sloughing wound resulted when the grafted area was "dry dressed." As emphasized in the text, it should be kept moist with glycerine, acetic acid, and saline solution when grafting immediately after resecting an infected ulcer. The wound was cleaned with penicillin urethane solution and a second graft applied, and the dressings kept wet. *A*, Sloughing wound following saphenous ligation and stripping, excision of an infected indolent ulcer, and skin grafting. *B*, Result of second skin graft.

Bone is customarily resurfaced with a full-thickness, cross-leg, pedunculated graft or even a migratory graft of the tubular variety. However, the exposed bone area, in the cases of chronic indurated cellulitis, is usually relatively small, and the split-thickness skin graft has proved entirely adequate, with the saving of many days of hospitalization for the patient.

Modification D: Surgical Technique for Chronic Indurated Cellulitis and Varicose Veins.—The saphenous vein is ligated at the femorosaphenous junction. This incision is radically high, 1 to 3 cm. above the crease in the groin. After dividing the superficial fascia, the saphenous vein is exposed by retracting

the lower border of the incision. The vein is divided and the proximal end dissected to its femoral junction. The "above the crease" incision places the femorosaphenous junction in the middle of the wound and affords excellent exposure for dissection and division of all the junction branches. The long saphenous vein is then stripped out using either the extraluminal Mayo strippers or the new flexible intraluminal strippers of Myers. It is not necessary to carry the stripping much below the knee level, for the lower branches are resected as one proceeds at once with surgical removal of the area of chronic indurated cellulitis or ulceration as previously described. When the short saphenous vein is varicosed or stasis ulceration exists on the outer aspect of the lower leg it is likewise ligated in the popliteal space (Fig. 10, *A* and *B*).

A. *B.*

Fig. 10, *A* and *B*.—Chronic indurated cellulitis and indolent leg ulcer from repeated attacks of thrombophlebitis in varicose veins. The long saphenous vein was stripped from groin to below the knee. The remaining saphenous varicosities, the indurated subcutaneous tissue, the fascia, the ulcer, and adjacent skin were resected. *A*, preoperative; *B*, postoperative.

Modification E: Surgical Technique for Chronic Indurated Cellulitis, Varicose Veins, and Incompetent Deep and Communicating Veins.—In this group of cases, there is a history of past iliofemoral thrombophlebitis. The saphenous system, overburdened during the deep vein obstruction, has become permanently varicosed. The femoral system has recanalized but is incompetent. The communicating veins are distended by a backflow of blood in both the saphenous and the femoral systems.

We have been following the work of Linton[5] in these cases. Previous experience had taught us that the superficial femoral vein and the long saphenous

vein can frequently both be divided with no untoward sequelae. Thus, on 2 occasions in operating for pulmonary embolism, we found clots in both the saphenous and femoral systems and performed a thrombectomy in each and ligated and divided the superficial femoral vein and the saphenous vein. On 2 other occasions, when a high saphenous ligation was followed by signs of phlebothrombosis in the calf, a superficial femoral ligation was subsequently performed. In none of these cases has there been any unusual leg edema or other evidences of chronic venous insufficiency. Serious venous insufficiency has not occurred in the 12 cases in which we have performed a superficial femoral ligation, a high saphenous ligation, and a vein stripping for the postthrombophlebitic syndrome as recommended by Linton. Our procedure has differed from Linton's only in that we discontinue the stripping just below the knee and perform from this level down a modified Kondoleon procedure to remove the pathologic subcutaneous tissue and fascia, resect the distal saphenous branches, and interrupt the communicating veins as previously described (Fig. 11, *1*, *2*, and *3*).

The technique in this group of cases is as follows:

1. In the same field, through a vertical incision below the crease in the groin, the saphenous vein and the femoral vein are exposed.

2. The venous pressure in the superficial femoral vein is taken while temporarily occluding the superficial femoral vein at its junction with the profunda and occluding the saphenous vein at its junction with the common femoral vein. Should the venous pressure not rise above 30 cm. in saline solution, both the superficial femoral and the saphenous veins should be ligated. If the venous pressure rises above 30 cm. in saline solution either the superficial femoral vein or the saphenous vein should be ligated, but not both.

3. The saphenous vein is stripped to below the knee (if it has been ligated in step 2). It is especially important in these cases to strip both the superficial and subfascial branches of the long saphenous, as pointed out by Sherman.[7] Unless this is done, incompetent perforators between the subfascial saphenous trunk and the femoral system will be missed.

4. The surgical removal of the area of chronic indurated cellulitis or indolent ulceration is continued as described in previous sections of this paper (Fig. 12, *A*, *B*, *C*, and *D*).

Several points merit attention in the postoperative management of chronic indurated cellulitis: the foot of the bed should be elevated 6 inches to prevent edema and venous stasis. Anticoagulant therapy is begun with heparin 4 to 6 hours after surgery and is maintained subsequently with Dicumarol until the patient is ambulatory. We feel that anticoagulant therapy has been of definite value in preventing embolism and only once have we had bleeding that caused complications (hemorrhage under the skin graft). When the patient becomes ambulatory, the sine qua non of success is adequate prevention of leg edema. Swelling of the leg will invariably break down the wound or the graft. A 4 inch wide Ace No. 8 leg bandage will usually suffice to prevent leg swelling. Such support should be worn until the tendency to edema disappears, a period of 4

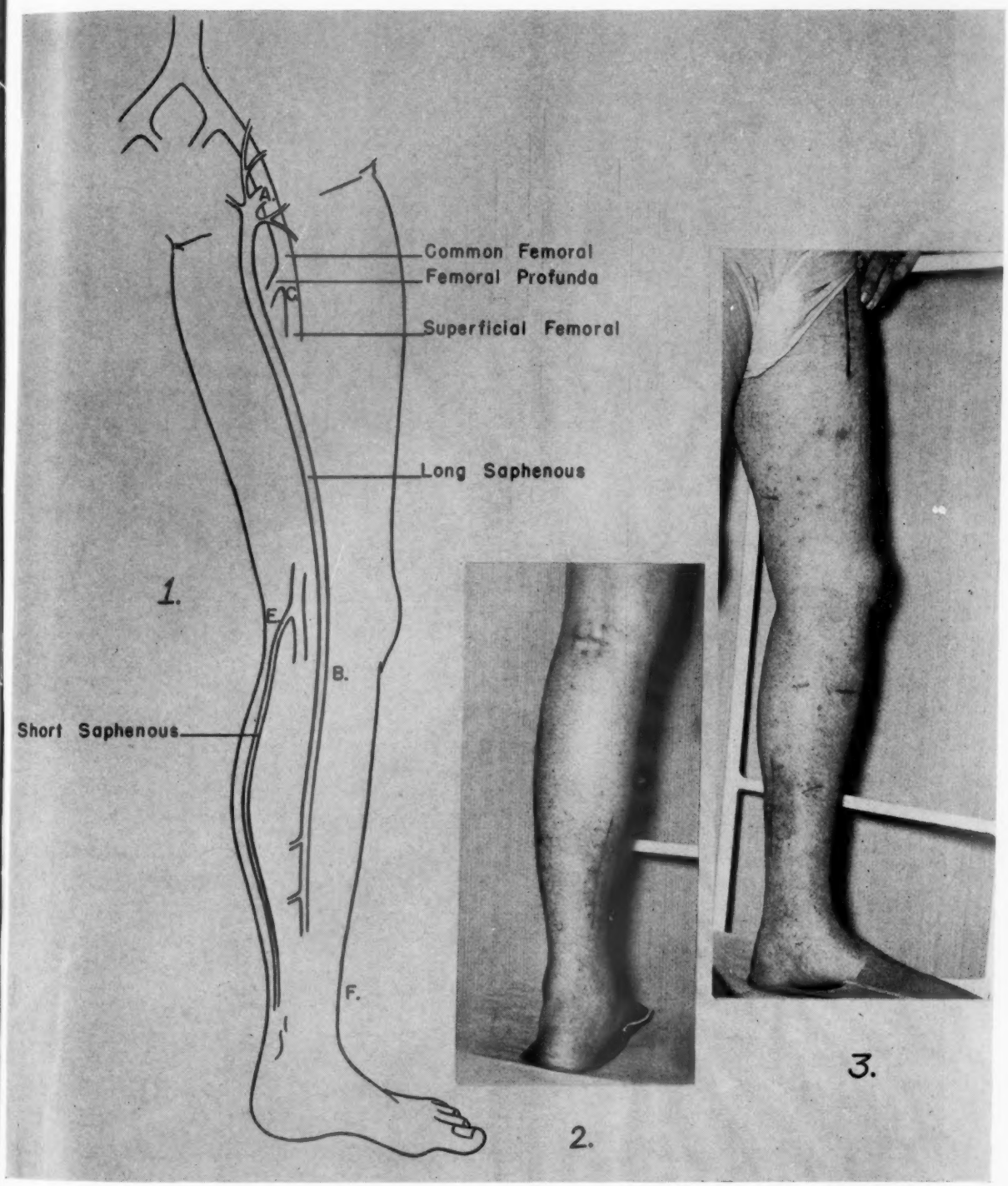


Fig. 11.—Illustrating the concomitant vein surgery that often has to be performed along with the chronic indurated cellulitis operation. *1*, The saphenous is ligated at *A* and removed by stripping from *A* to *B*. The short saphenous is ligated at *E*. The superficial femoral is ligated at *C*. The saphenous branches and incompetent perforating veins in the area *B* to *F* are resected during the subsequent "indurated leg operation." *2*, Showing the incisions for ligating the short saphenous vein and performing the indurated leg operation. *3*, Showing the incisions for ligating and dividing the long saphenous and superficial femoral veins and resecting by stripping of the entire long saphenous system.

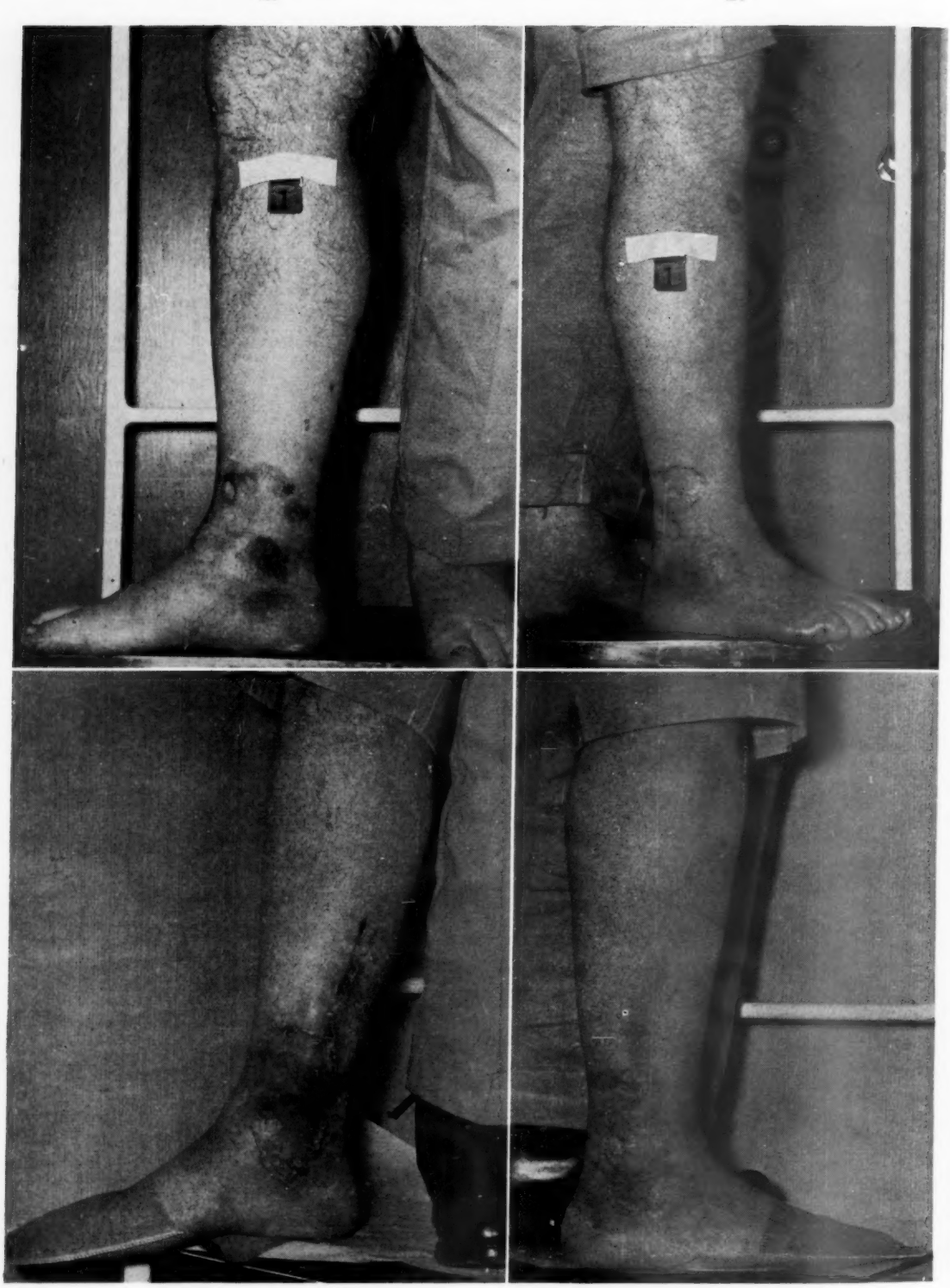


Fig. 12, *A*, *B*, *C*, and *D*.—Postthrombophlebitic chronic indurated cellulitis complicated by repeated episodes of localized thrombophlebitis in varicose veins. Treatment consisted of long and short saphenous ligation, superficial femoral vein ligation, excision of the indurated tissue on inner and outer aspect of the ankle, and skin grafting. *A* and *B*, inner and outer aspects of leg before operation; *C* and *D*, inner and outer aspects of leg after operation.

to 6 months. There are many tricks to the aftercare of these patients in order to prevent dermatitis and to obtain a complete healing, but with experience these are soon learned.

DISCUSSION

The therapy of chronic indurated cellulitis requires wide and radical removal of all pathologic tissues, skin, subcutaneous fat, and fascia. To compromise by leaving en situ some of the areas of diseased tissue spells failure as surely as would a similar procedure in the radical treatment of cancer. Where skin grafting is necessary, the wider and more complete the removal of damaged tissue, the better will be the take of the graft and the more sure its permanency. A graft surrounded by scar tissue is bound to break down in time.

The pathology of chronic indurated cellulitis never involves the underlying muscle. No matter how bad the leg looks there is a normal leg with healthy, well-vascularized muscles underneath. Excise the damaged tissue, apply immediately normal skin to normal muscle, correct any co-existing venous disturbance causing circulatory stasis, and the patient with chronic indurated cellulitis can be permanently rehabilitated.

Measures to correct the venous stasis—saphenous ligation and stripping, superficial femoral or popliteal vein ligation, femoral vein resection—cannot be expected alone to correct the pathology under discussion. Irreversible pathology exists in the lower leg and correction of the presumed cause can no longer alter its status. When varicose veins are present, saphenous ligation and stripping seem rational as part of a composite operation for the indurated leg. Further experience and a longer follow-up period seem indicated to evaluate the effects of concomitant femoral or popliteal ligation.

This paper is based on approximately 110 cases. The majority of these patients have been operated upon during the past 4 years. Although we had performed somewhat similar procedures prior to this time, our present radical approach and the associated procedures and details have crystallized only during the past 4 years. The immediate results have been good. About 75 per cent of the primary skin grafts take 100 per cent. The grafting is relatively an unimportant phase of the procedure. Once the underlying pathology has been eradicated, one can always eventually cover a remaining defect with skin. When part of a graft fails to survive, often all that is necessary is the application in the patient's room or in the emergency room of a few Davis pinch grafts obtained under local anesthesia.

Only 5 recurrences are known to have occurred and follow-up data is fairly complete. In addition to many grateful private patients, it has been a pleasure to eliminate a large list of "chronics" in the vascular clinic. Endless dressings, elastoplast bandages, Unna paste boots, and ineffectual local medication have been replaced by definitive surgery.

There have been 3 instances of pulmonary embolism, all before we began the routine prophylactic use of anticoagulant therapy. Two occurred while the patients were still in the hospital, 1 a few days after hospital discharge. An iliac ligation on the previously operated side and a femoral ligation on the

opposite side were performed in the first instance. The second case was recognized late and the patient was treated with anticoagulant therapy. The third patient was rehospitalized and a bilateral superficial femoral ligation performed with thrombectomy on the affected side. All three patients recovered.

There has been no mortality, and no recognizable instance of pulmonary embolism has occurred since we have instituted routine prophylactic anticoagulant therapy. Hospital stays have varied from 2 to 6 weeks.

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PILONIDAL CYST: A COMPARISON OF SURGICAL TREATMENTS

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INTRODUCTION

THIS study of the pilonidal cyst and sinus is based on operative experience with approximately 800 cases of this disease treated at the Halloran Veterans Administration Hospital since Jan. 1, 1947. The results as reported here, however, are limited to the 584 patients on whom follow-up of three to thirty months is available.

This paper is a comparative evaluation of the healing times, using the various techniques as practiced at this hospital. The cases reported herein represent the results of the work of the entire surgical staff. A later paper will report on the follow-up results.

There appears no justification for a lengthy discussion of etiology or pathology of this disease at this time. Emery has written an excellent monograph[1] with an exhaustive study of the etiology, incidence, and pathology of the pilonidal cyst, and a review of some of the many techniques of therapy being used for the treatment of this disease.

TECHNIQUE

As will be seen from the accompanying tables, all cases are divided into two groups: (1) quiescent, and (2) infected. Since almost 100 per cent are actually infected, this represents a rough clinical separation of the degree of infection. A cyst is "infected" if pus is noted and/or more than a minimal amount of induration is present. Acute abscesses are not included; these are incised and drained, and excisional therapy delayed 4 to 6 weeks.

Nonoperative Treatment.—No injections of caustics[2] or other materials designed to destroy the cyst have been attempted at this hospital.

Operative Therapy.—Open packing: Excision and open packing has been done in the past, by some of the staff, for any of the so-called "infected" cases. The disease tissue is excised, and the wound packed open with petrolatum, iodoform, or dry gauze. The packing is removed on the third to seventh postoperative day, and the patient started on sitz baths three times daily. When the wound appears clean and is granulating well, the patient is sent home on a routine of daily sitz baths and dressings, and returns to the hospital about once a week for dressings. Hospital discharge is usually on the sixteen or seventeenth postoperative day. Most of the house staff have abandoned the open packing (for reasons as noted below) except for two types of cases: (1) where the cyst is too large to permit closure without excess tension, or (2) where the cyst extends down to the anal sphincter.

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Delayed or secondary closure: This technique has been used in only a few cases here, mostly to correct the asymmetry of the edges of the granulating wound of a previously excised cyst. The results, shown in Table I, are poor; the usefulness of this technique appears limited.

TABLE I. HEALING DATE OF ALL CASES INCLUDED IN THIS STUDY

TECHNIQUE	TYPE OF CASE	PER PRIMAM	DAYS						
			LESS THAN 30*	30 TO 60	60 TO 90	90 TO 120	120 TO 150	OVER 150	OVER 60 UNKNOWN†
Primary Closure (409 cases)	New‡								
	Quiescent	175	14	11	3	2	2	3	6
	Infected	121	5	9	5	2	0	6	3
	Recurrent								
	Quiescent	17	0	2	0	1	0	0	1
	Infected	12	0	1	0	2	0	1	0
	Total								
	Quiescent	197	14	13	3	3	2	3	7
	Infected	133	5	10	5	4	0	7	3
Secondary Closure§ (16 cases)	New								
	Quiescent	3	2	0	1	0	0	1	2
	Infected	1	0	1	1	0	0	1	0
	Recurrent								
	Quiescent	0	0	1	0	0	0	0	1
	Infected	0	0	1	0	0	0	0	0
	Total								
	Quiescent	3	2	1	1	0	0	1	3
	Infected	1	0	2	1	0	0	1	0
Open Packing (159 cases)	New								
	Quiescent	0	0	3	7	4	2	0	12
	Infected	0	1	20	19	9	8	11	21
	Recurrent								
	Quiescent	0	0	1	2	1	0	1	4
	Infected	0	0	5	7	7	2	9	3
	Total								
	Quiescent	0	0	4	9	5	2	1	16
	Infected	0	1	25	26	16	10	20	24

*Patients in whom healing was not per primam, but occurred by the thirtieth postoperative day.

†"Over 60 unknown" includes those patients whose exact healing date could not be determined, but on whom it apparently required more than 60 days.

‡The term "new" indicates patients on whom no previous excisional surgery had been performed.

§Healing time measured from date of excision.

Primary closure: Numerous methods and techniques, all with individual variations, have been tried. The results of the major groups of techniques used on these primarily closed cysts are tabulated in Table II. The techniques are as follows:

(1) Mobilization of muscle and fascial flap: Sixty-eight cases of this series have been done by mobilization of muscle and fascial flaps and approximation of these flaps to fill the dead space left by excision of the cyst, essentially as described by Holman.[3] There seems to be some increased difficulty in controlling bleeding and some hematoma formation, as well as the disadvantage of buried suture, as noted later, in the performance of this type of primary closure.

(2) Buried catgut or cotton: Buried catgut or cotton to obliterate the dead space (without mobilization of flaps) was used in seventy-nine cases. Of these,

TABLE II. VARIOUS TECHNIQUES OF PRIMARY CLOSURE (INCLUDING ONLY THOSE CASES DONE WITH ONE OF THE FOUR MOST USED TECHNIQUES)

TECHNIQUE	TYPE OF CASE		PER PRIMAM	DAYS		PERCENTAGE HEALING	
				LESS THAN 30	OVER 30	PER PRIMAM	TOTAL WITHIN 30 DAYS*
Buried cotton suture with silk skin suture	New						
		Quiescent	16	1	6		
		Infected	2	1	2		
	Recurrent						
		Quiescent	1	0	1		
		Infected	0	0	0		
	Total					63.4	70.0
		Quiescent	17	1	7		
		Infected	2	1	2		
Buried catgut suture with silk skin suture	New						
		Quiescent	11	0	4		
		Infected	22	2	5		
	Recurrent						
		Quiescent	3	0	1		
		Infected	1	0	1		
	Total					74.0	78.0
		Quiescent	14	0	5		
		Infected	23	2	6		
Muscle and fascial flap, with buried catgut and silk skin or subcuticular tantalum	New						
		Quiescent	24	6	7		
		Infected	18	0	10		
	Recurrent						
		Quiescent	2	0	0		
		Infected	1	0	0		
	Total					66.2	75.0
		Quiescent	26	6	7		
		Infected	19	0	10		
Steel skin and retention sutures	New						
		Quiescent	113	5	14		
		Infected	79	2	7		
	Recurrent						
		Quiescent	11	0	1		
		Infected	10	0	2		
	Total					87.4	90.2
		Quiescent	124	5	15		
		Infected	89	2	9		

*Total within 30 days includes per primam healing plus those patients in whom the wound healed by secondary intention within 30 days from date of operation.

fifty-six healed per primam. The use of this technique (and of the flap technique) has the disadvantage that foreign material is being buried in a nonsterile area.

(3) Metallic skin sutures with no buried material: The use of metallic (steel) skin and retention sutures, without any buried material (except ligatures) is the method which has proved most satisfactory in our hands. The technique is not claimed as original, but a search of the literature fails to reveal any previous description of it.

All cases are done under spinal anesthesia, with the patient acutely flexed. and on his abdomen. An elliptical incision is made and carried down to the presacral fascia, and all the grossly diseased tissue is removed. Hemostasis is obtained by clamping and ligation of the larger vessels (using 00 plain catgut), and the cavity washed out with warm saline solution. At this point, the decision with regard to closure is made, depending on the size and location of the wound,

TABLE III. SYSTEMIC PENICILLIN THERAPY IN PRIMARY CLOSURE (INCLUDING ONLY THOSE CASES DONE WITH ONE OF THE FOUR MOST USED TECHNIQUES)

TECHNIQUE	TYPE OF CASE	PER PRIMAM	DAYS: LESS THAN 30	DAYS: OVER 30	TOTAL CASES	PERCENTAGE HEALING: PER PRIMAM	PERCENTAGE HEALING: TOTAL WITHIN 30 DAYS
Steel wire suture	New						
	Quiescent	42	2	2			
	Infected	22	0	2			
	Recurrent						
	Quiescent	3	0	0			
	Infected	4	0	1			
	Total				78	91.1	93.5
	Quiescent	45	2	2			
	Infected	26	0	3			
Buried cotton or catgut or muscle flap technique	New						
	Quiescent	51	7	17			
	Infected	42	3	17			
	Recurrent						
	Quiescent	6	0	2			
	Infected	2	0	1			
	Total				148	68.3	75.0
	Quiescent	57	7	19			
	Infected	44	3	18			

as noted previously. It should be noted here that the degree of infection, barring only the acute abscesses, has not been a factor in the decision of primary closure versus open packing in our cases in the past eighteen months. If closure is to be performed, heavy steel (0.014 or 0.015) wire sutures are then placed through the presacral fascia and brought out 3 to 4 cm. lateral to the wound edges. Fine steel (0.007 or 0.009) sutures are then placed in vertical mattress fashion, getting either just skin and subcutaneous tissue (65 per cent of cases), or including a bite of presacral fascia, according to the preference of the operator. (No difference in results due to these minor variations of technique can be demonstrated.) The skin sutures are then tied, a large gauze roll is placed over the suture line, and the previously-placed retention sutures tied tightly over the gauze roll. The gauze roll is of such size as to allow the retention sutures to be tied sufficiently tight to obliterate any potential dead space without excess tension on the skin. The patients are ambulated six hours postoperatively. The sutures are removed on the seventh to eighth postoperative day and the patient leaves the hospital on the tenth to eleventh postoperative day. He is advised to avoid sitting for one to two weeks posthospital discharge.

Most of the closures have been done in a longitudinal direction, since this is usually the long axis of the cyst. Four cases required transverse closure, and this was done. All four healed per primam and have remained healed.

Of this series, 245 patients have been operated upon using this technique, or with minor modifications thereof. Of these, 213 cases (87.4 per cent) healed per primam, and an additional seven cases healed within thirty days after operation. The cases which are not included in this report, either because they have been lost on follow-up or because they are of too-recent performance, do not appear to differ in any significant fashion in their percentage of primary healing.

TABLE IV. ADJUVANT THERAPY USED WITH THE STEEL WIRE CLOSURE

TECHNIQUE	TYPE OF CASE	PER PRIMAM	DAYS		PERCENTAGE HEALING	
			LESS THAN 30	OVER 30	PER PRIMAM	TOTAL WITHIN 30 DAYS
Systemic penicillin (78 cases)	New					
	Quiescent	42	2	2		
	Infected	22	0	2		
	Recurrent					
	Quiescent	3	0	0		
	Infected	4	0	1		
	Total				91.1	93.5
	Quiescent	45	2	2		
	Infected	26	0	3		
Insufflation of penicillin-sulfonamide, streptomycin powder (102 cases)	New					
	Quiescent	44	3	3		
	Infected	40	2	3		
	Recurrent					
	Quiescent	4	0	0		
	Infected	3	0	0		
	Total				89.2	94.2
	Quiescent	48	3	3		
	Infected	43	2	3		
No adjuvant therapy (65 cases)	New					
	Quiescent	31	1	6		
	Infected	9	1	5		
	Recurrent					
	Quiescent	6	0	2		
	Infected	3	0	1		
	Total				75.4	78.5
	Quiescent	37	1	8		
	Infected	12	1	6		

Nonoperative Supplementary Treatment.—It is our usual practice to encourage drainage of the cyst preoperatively by the use of sitz baths and insertion of a wick drain. The effect of this appears to be negligible, and surgery is not held up for this type of preoperative preparation.

Acute abscesses are treated by incision and drainage and the patient is sent home. Excisional therapy is postponed for four to six weeks as noted previously.

The use of penicillin preoperatively did not materially effect the percentage of per primam healing in our cases.

Penicillin postoperatively, however, had a demonstrable effect on our statistics. Systemic penicillin (aqueous penicillin 30,000 U. q3h, or 300,000 U. per day of penicillin in oil or procaine penicillin) was used in 226 cases. The results of ths therapy may be seen in Tables III and IV. The use of sulfonamides with penicillin postoperatively did not have a measurable effect on the results.

The local use of chemotherapeutic agents also had a measurable effect on our results. Using the steel wire closure as described, 102 cases were treated, and a powder consisting of a mixture of penicillin, streptomycin, and the sulfonamides was dusted into the wound just prior to closing. The results in this group may be seen in Table IV.

Work on the local use of this powder in the pilonidal cyst and in other wounds is being done.*

*By Dr. P. W. Finney of our surgical staff.

CONCLUSIONS

The advantages of primary closure over open packing techniques appear to be as follows:

1. Hospitalization is shortened with primary closure (eleven days versus seventeen days for open packing) and, when the patient leaves the hospital, his wound is healed. With open packing, the patient is required to return for at least weekly dressings.

2. The patient "packed open" retains an open sacral wound for approximately seventy-five days (Table I); this wound requires special daily care (dressings and sitz baths).

In our experience, recurrences have not been greater (in our relatively short follow-up period) in this series of cases treated with primary closure. The results in this regard will be fully presented in a subsequent report.

The objection may be raised, of course, that the cases treated by open packing are, for the most part, the larger or more infected cysts. This objection, however, is only partially valid. It is to be noted that approximately 70 per cent of all cases reported here (done prior to July, 1949) were treated by primary closure, and that this has risen even higher in the cases done in the past year (to October, 1949). The degree of infection plays no part in the decision with regard to closure; the only limiting factors are the ability to oppose the skin edges without excess tension, and the location of the cyst.

Of the various primary closure techniques, the steel wire closure has given the best results in our hands. This technique was used in 245 cases (Table IV), with the results as indicated.

The use of antibiotics has varied, as has the use of various techniques, according to the preference of the individual operator. Postoperative penicillin was used in 226 cases, and these are classified in two groups in Table III. The steel wire method shows a definite statistical advantage. When the wire cases are broken down by antibiotic groups (Table IV) it is seen that the 78 cases with systemic penicillin and the 102 cases with local antibiotic show approximately the same rate of primary healing (approximately 90 per cent) and that both show a significant advantage over the no antibiotic group of 65 cases.

SUMMARY

A study of the various types of operative and adjuvant therapies used in the treatment of 584 cases of pilonidal cyst at the Halloran Veterans Administration Hospital is presented. Primary closure, using steel wire sutures and either penicillin systemically or a powder consisting of streptomycin, penicillin, and the sulfonamides locally gave the best results.

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DOUBLE-LUMEN T TUBE FOR THE COMMON DUCT

Continuous Drainage and Reintroduction of Bile in the Dog

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With the Technical Assistance of Lamar Walker

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FOLLOWING surgical drainage and intubation of the common bile duct, maintenance of nutrition is often deficient. Vomiting may occur, and venoclysis may be difficult and inadequate. To overcome this difficulty, Holsinger[1] has used an ingenious method for direct intestinal alimentation. With the ordinary T tube in place in the common duct, he pushed a No. 6 French catheter through its distal limb, the common duct, and the ampulla of Vater, into the duodenum. Holsinger has reported that 5 postoperative patients were adequately maintained, receiving fluids, minerals, proteins, vitamins, or lactate solution by this method. Cattell[2] has employed a conventional T tube with a long horizontal limb which passes into the duodenum through the ampulla of Vater. He has utilized this tube in the immediate postoperative period for alimentation with saline solution or glucose, obviating the need for intravenous fluids. This tube, however, is not effective in cholangiography because the contrast medium enters the duodenum immediately. Occasionally too, there is reflux into the biliary ducts from the duodenum with subsequent cholangitis, evidenced by malaise, chills, and fever. Irrigation to maintain patency and to avoid encrustation is routinely employed after the first week. This tube has been left in place for as long as eighteen months, and its removal has not been followed by untoward complications.

We have constructed a double-lumen T tube, which obviated introduction of a separate catheter for intestinal nutrition, and by which liver bile can be shunted into the upper intestine.* This tube has been found practical and useful in experiments on the dog.

The double-lumen T tube appears outwardly like the conventional T tube except that the distal limb is longer to allow for intubation of the duodenum through the common duct and the ampulla of Vater. The vertical part of the T tube has a double lumen, one branch of which leads to the proximal limb and the other branch into the distal limb (see Fig. 1).

EXPERIMENTS

Six mongrel dogs were used, ranging in weight from 12 to 25 kg. Aseptic operations were performed under sodium pentobarbital anesthesia. The biliary system was exposed by a right oblique incision, and cholecystectomy was performed. The common duct was incised in its mid-portion, the short end of the T tube was introduced proximally toward the liver, and the long distal end was pushed gently into the duodenum. The double lumen part of the tube was

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*We are indebted to American Cystoscope Makers for making this tube for us.

brought to the outside through a stab wound, and the abdomen was closed in three layers. Bile flowed immediately from the proximal limb, and intestinal secretions could be withdrawn from the distal limb. The two segments were joined outside of the animal's body with a polyethylene link of tubing to allow for continuous passage of bile into the duodenum. The postoperative care was as follows: 200 c.c. of 5 per cent glucose in Ringer solution was given into the distal limb of the T tube by slow drip on the second postoperative day. While the solution was administered, bile was collected from the proximal limb. The collected bile was returned by gravity flow into the distal limb. This procedure was repeated for one or two additional days. On the third and fourth postoperative days, 2 ounces of protein hydrolysate were added to the glucose Ringer solution. Thereafter, milk, vitamins, and human plasma were administered through the tube, and the animals were permitted water and food by mouth.

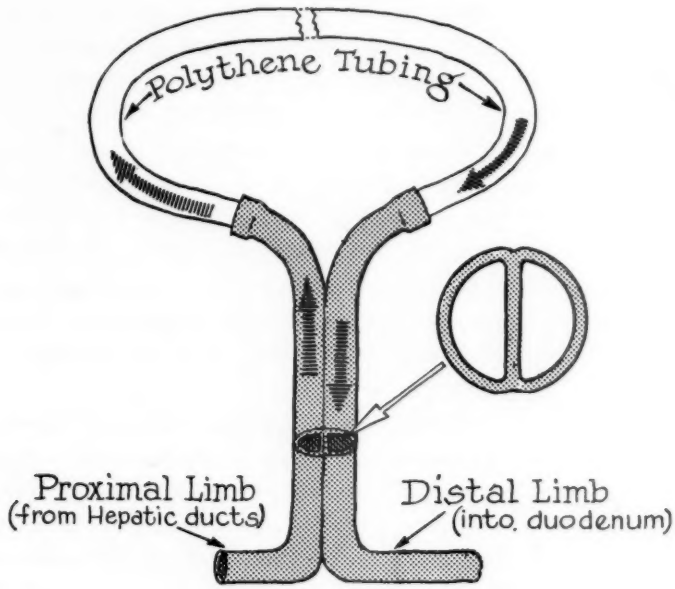

Fig. 1.

The tubes were removed without incident on the fourteenth postoperative day. The dogs were sacrificed on the twenty-first day after operation and autopsied. No evidence of ill effects which could have been ascribed to the use of this tube was found. The average serum bilirubin postoperatively was 0.25 per cent. No animal developed jaundice or appeared ill, and they were able to take water and food by mouth. Choledochograms were done on several of the dogs, using both proximal and distal limbs.

DISCUSSION

Another possible method of accomplishing the same effect as with the double-lumen T tube would be the use of 2 individual catheters. This was found unsatisfactory because separate fistulas formed, due to angulation of these tubes. This we have seen in our early experimental work, where our improvised double-lumen T tubes were no more than 2 individual catheters tied together.

Holsinger[1] has stressed the difficulty in maintaining nutrition during the first few days after cholecystectomy, and we feel that our double-lumen T tube offers advantages for that purpose. Feeding through the conventional T tube is not a safe procedure because of possible contamination of the ascending biliary tree and because the pressure necessary at times to force nutrient substances through the ampulla of Vater may produce liver damage by increased pressure in the bile radicals. Separate choledochograms can be made with the double-lumen T tube of the intra-and extrahepatic biliary trees.

With the double-lumen T tube one can establish either a constant bile flow into the duodenum by connecting the proximal and distal limbs, or one may collect the bile from the proximal limb and inject it later into the duodenum through the distal limb. The bile flow can be determined quantitatively and qualitatively, and the patient's own bile can be administered into the duodenum at mealtime.

By the use of the double-lumen T tube, dogs were maintained in a good state of nutrition and hydration. We have seen no technical disadvantage in the use of the double-lumen T tube experimentally, compared to the conventional T tube. In the dog the double-lumen tube is as easy to insert as the conventional T tube, and its removal is as easy and appears to have no more hazards or complications. It is possible that a spasm of the sphincter of Oddi may prevent admission of the distal limb of our tube into the duodenum, but dilation or surgery of the sphincter[2] or the use of spasmolytic drugs[3] may circumvent this difficulty. A further advantage in the use of the double-lumen T tube may be in decompression of the upper small bowel in postoperative ileus. This has been tested in the dog and found practical.

SUMMARY

1. A double-lumen T tube has been used experimentally in the dog with success, and is recommended for clinical application.

2. The advantages of this tube over the conventional T tube or the long T tube with respect to nutrition, cholangiography, intermittent or constant bile flow into the duodenum, collection of bile, and for duodenal aspiration have been described.

3. No ill effects or undue symptoms were seen in the dog with the use of this tube.

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THE BROWN ELECTRODERMATOME; A NEW INSTRUMENT

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THE technique of skin grafting has been simplified in recent years by the development of the Padgett dermatome and its modifications by Reese. This instrument allows for precise removal of large skin grafts of an accurate predetermined depth. It does require the use of adhesive substances both on the skin and on the surface of the dermatome. The movement of the blade is carried out by the operator, and the success of skin removal depends in part on adhesive substance of proper type. Excess atmospheric humidity or excess skin moisture can interfere with the successful removal of the graft.

The Brown electrodermatome is a recent mechanical development in dermatomes and is a most ingenious one. It was designed by Dr. Harry Merrill Brown of Indianapolis, Ind., who was killed in an automobile accident in the summer of 1948. Brown conceived the idea of an electrodermatome while he was a prisoner of war in the Philippine Islands, and upon his return to the United States he perfected this instrument, in conjunction with Mr. Milford Baron.

The instrument is simple in design, resembling an ordinary hair clipper (Fig. 1). No adhesive substances are used. The skin of the donor area is simply covered with a light film of mineral oil, and the graft is then removed. Firm pressure is made while taking the graft without fear of increasing its depth to subcutaneous levels. The thickness of the graft to be taken can be accurately set by an adjustable guard, and disposable blades are used. The cutting head and its long shaft can be sterilized, then screwed on the motor.

It has several disadvantages in comparison with the Padgett-Hood dermatome and also with the Reese modification. Although there is no limit to the length of graft other than anatomic factors, the widest graft that it can remove is a 3 inch one. The Padgett-Hood-Reese instrument will remove a graft 4 inches in width. It does not lend itself as readily to the taking of pattern grafts as is possible with the Padgett-Hood-Reese instrument. No splinting effect of the rubber backing is available as in the Reese modification, but we have not felt this factor to be significant in the "take" of skin grafts, although it does prevent the 20 per cent shrinkage ordinarily occurring after the removal of the skin. This can be overcome by suturing of the graft removed with the Brown instrument.

Our personal experiences with the instrument over the past year have been most satisfactory both as to the quality of the graft and its simplicity of removal. It has not completely replaced the Padgett-Hood-Reese instrument, principally because of the fact that the graft is 1 inch narrower. It is of real

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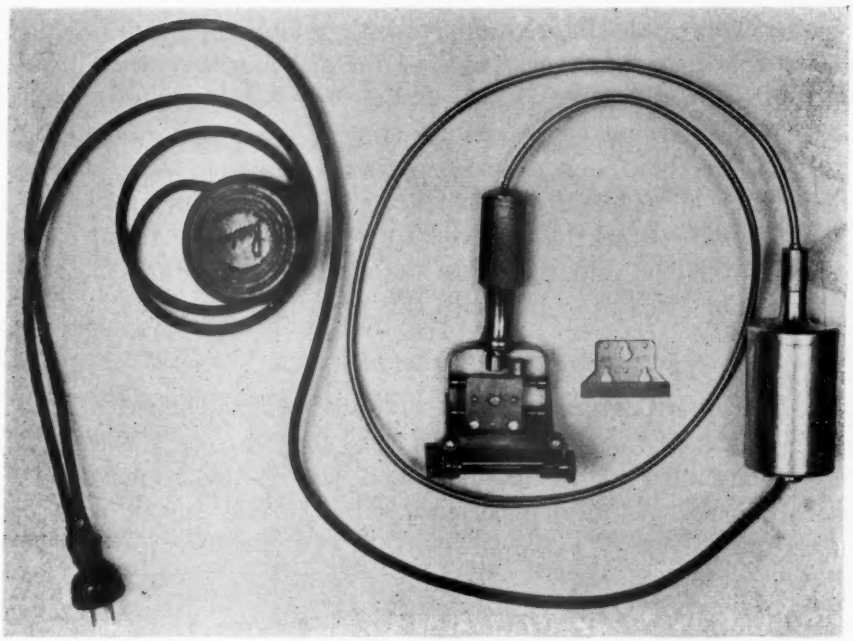

Fig. 1.—The Brown electrodermatome. Left to right are shown the footswitch, the dermatome, the blade, and the motor.

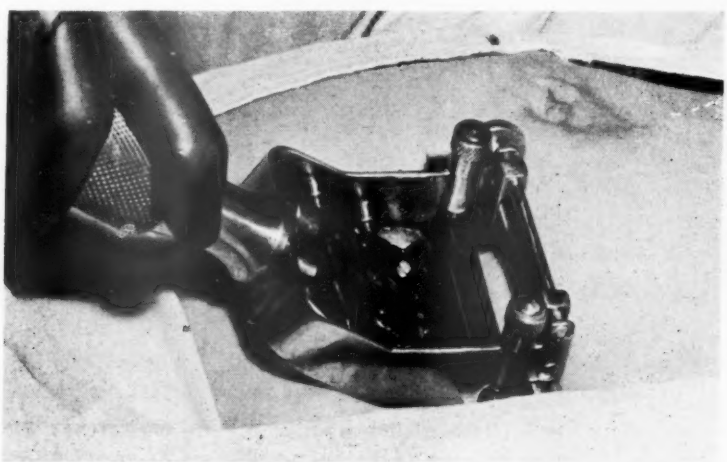

Fig. 2.—The dermatome in place against the skin ready to use.

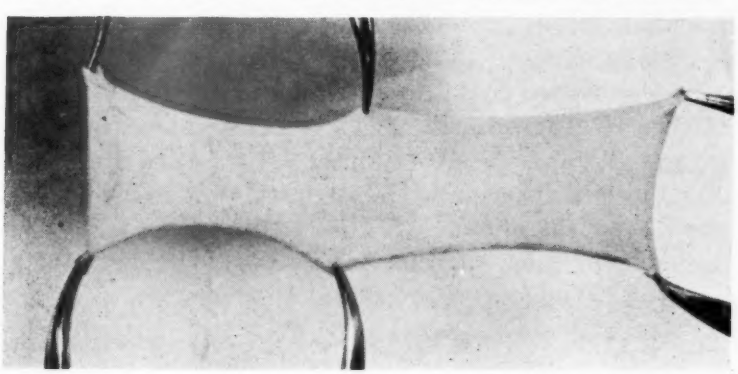

Fig. 3.—Graft removed with the Brown electrodermatome.

value in cases where this differential in width is not important. It is also of value on a surgical service where the need for grafting may occur in a variety of circumstances by a variety of operators. The occasional skin grafter will be grateful for its accurate removal of skin by a method outstanding in its simplicity. It has been our experience that a surgeon, after two to three minutes' instruction, can remove a perfect graft on his first use of the instrument. The "take" of grafts removed by the Brown electrodermatome has been most satisfactory, and there has been no evidence that the mineral oil used on the donor area interferes with this most important factor.

CONCLUSION

The Brown electrodermatome is a motor-driven instrument of new design with oscillating blade for the removal of skin for grafting. The technique of removal is outstanding in its simplicity and can readily be mastered with no previous experience. Clinical experience with the instrument has resulted in excellent results.

A NEW BAYONET CLAMP FOR HIGH GASTRIC RESECTION

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IN THE performance of gastric resection for either ulcer or carcinoma, an attempt should be made to resect as much of the stomach as is technically feasible. If the mobilization of the stomach permits, a clamp can be used on the proximal gastric end, above the level of the anastomosis, to prevent spillage of the gastric content into the peritoneal cavity.

The characteristics of such a clamp should be that it is manageable enough not to injure the stomach wall, that it should be made in such a manner that it will not slip, and that it be of such a shape that it can be introduced into the abdomen so that the site of the resection and anastomosis can be at a deeper level than the abdominal wall. Such a clamp has been in use in my clinic since 1942, and has been successfully employed in over 500 gastric resections.

Fig. 1.—The clamp is bayonet shaped. The branches are encased in rubber tubing, and in the apex there is a small hinged lock to prevent slipping.

After the duodenum has been severed and cared for in the usual manner, mobilization of the stomach is completed high on both the lesser and greater curvature by ligation of the vessels. This mobilization may be carried almost to the esophagus on the lesser curvature, and high enough on the greater so that well over three-fourths of the stomach is resectable. The clamp is then applied. The end is locked by the small hinged lock on the apex of the clamp. A second clamp is then applied more distally on the stomach. This may be a crushing type or any other type. The subserosal vessels are then secured with fine suture material. In a deep, yet dry, field, the anastomosis may then be performed. It may be either the entire width of the resected stomach, or with a partial closure of the gastric end after the technique of Hoffmeister-Finsterer. The stomach is then removed.

It will be noted that the anastomosis will of necessity require the use of curved needles, as the anastomosis will be done deep in the abdominal cavity. This, while adding slightly to the technical difficulties of the operation, insures that an adequately high resection is being performed, and will certainly add to the beneficial results of the operation. To perform the same resection without the clamp means that an open resection must be done. This is technically difficult, is obscured by a bloody field, and permits spillage of the gastric content.

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Case Reports

ECTOPIA CORDIS

A Case Report

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ECTOPIA cordis is a rare anomaly characterized by extrathoracic displacement of the heart. Reviews of the literature in recent years by Barlow,[1] Roth,[2] Blatt and Zeldes,[3] and Byron[4] record 142 cases, and we have noted reports of four others[5-8] to which we are adding a fifth. The first description has been variously accredited to Haller and to Marinez, both of whom reported cases in 1706. However, Willius[8] has recently cited a report by Niels Stensen, the great Danish physician and anatomist, whose article, in 1671, included a description of the so-called tetralogy of Fallot. Although Stensen's report clearly describes the dissection of an embryo monster with ectopia cordis, it has not been mentioned in any of the previous reviews on this subject.

Abbott[9] defines ectopia cordis as "a displacement so that the heart passes out of the thorax and comes to lie either upon the outer surface of the body or in the abdominal cavity." In general, these cases can be segregated into three main groups, cervical, thoracic, and abdominal, but in some instances the position of the heart may overlap two of these regions.

Though the etiology of the defect is unknown, various authors have advanced theories to explain its pathogenesis. The theory receiving the greatest embryologic support is that of failure in the normal closure of the parietes due to an inherent defect in the dorsal plate of the myotomes. In some cases there is an associated failure to constrict and occlude the early physiologic omphalocele, and in many instances internal anomalies of the heart and of the great vessels have been noted.

The prognosis of the child with an externally displaced heart is poor. The majority of cases have died within a few days. Abdominal ectopia, on the other hand, is compatible with a normal life span, as illustrated by Ramire's case[3] of a man who died at the age of 75 years.

Attempts at operative correction of externally displaced hearts have so far been unsuccessful. Cutler and Wilen[10] and Byron[4] tried replacing the heart within the thorax, while Bloch[11] and Hoffman[12] attempted to cover the organ by means of skin flaps. The report of Burton[13] on a "Method of Correction of Ectopia Cordis" is misleading, since his patients had only partially bifid sternal bones with intact overlying skin and no significant cardiac displacement, and therefore they could not be included under Abbott's definition of ectopia cordis.

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During the survival period of infants with ectopia cordis, the physician has an excellent opportunity to observe the heart's action. Electrocardiographic tracings have been recorded by a number of authors.[1, 3, 14-17]

CASE REPORT

The child was an Arab male infant admitted to the American University Hospital on July 28, 1948, having been born at home fourteen hours previously. The parents and two siblings were living and well; none of them had any known anomalies. Physical examination revealed a complete extrophy of the heart, which projected forward from the chest and struck against the chin with each beat. The pericardial sac was absent, being represented merely by a small plaque of serous membrane posterior and inferior to the heart. The sternum was split in its lower portion but appeared fused in the manubrial region. There was an associated omphalocele, which contained liver and intestines. The remainder of the examination was negative except for the presence of bilateral talipes equinovarus. A motion picture in color of the heart action was made.

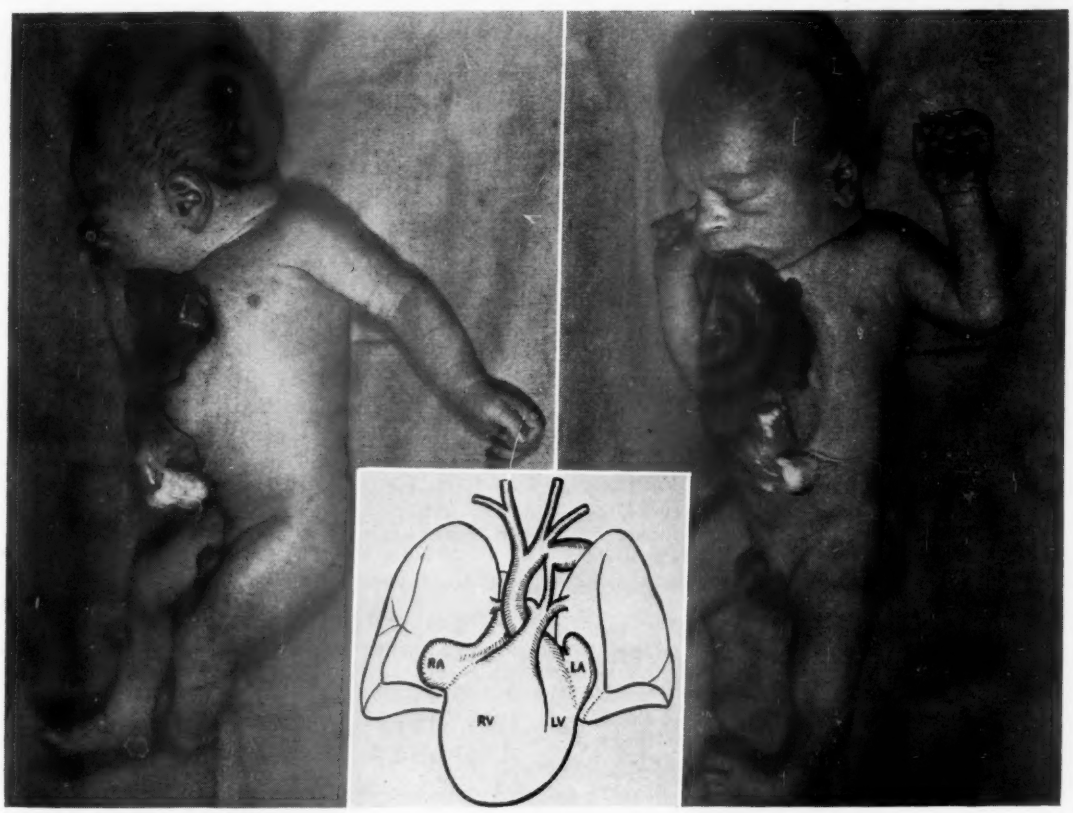

Fig. 1.—Lateral and ventral views of the patient showing the extrathoracic heart and large omphalocele. Inserted diagram of the heart and great vessels demonstrates the patent ductus arteriosus and coarctation of the aorta.

Shortly after admission, the child was taken to the operating room, and an attempt was made to cover the heart with skin flaps. Local anesthesia was used, and oxygen was administered by nasal catheter. The principles outlined by Ladd and Gross[18] for the repair of large omphaloceles were followed, and the abdominal portion of the defect was closed without difficulty. However, cardiac embarrassment developed each time the skin flaps were drawn over the heart. An attempt to place the heart beneath a subcutaneous pocket in the neck also resulted in rapid weakening of its action. Gradual adjustment of the heart to these

positions was likewise unsuccessful, so the operation was discontinued. The heartbeat remained weak and in the course of the next hour gradually failed in spite of stimulants.

Autopsy Findings.—The body was that of a male infant, weighing 2,570 Gm., with a crown-heel length of 44 cm. The sternum was found cleft and flaring widely up to a point 5 cm. below its superior notch. A defect in the anterior body wall extended from this level to the hypogastrium, 8 cm. below the diaphragm. The skin edges of the defect were freshened and sutured up to the level of the diaphragm. The right and left ventricles and a part of the diaphragm presented through the upper part of the defect. The anterior surfaces of the heart and liver were covered by a thin layer of grayish, dull material.

The heart showed some right ventricular hypertrophy and dilatation. An anatomically open foramen ovale was closed by overlapping leaves of endocardium. The ductus arteriosus was patent, and there was a coaretation of the aorta between the origin of the left subclavian artery and the attachment of the ductus (Fig. 1). The gross examination was otherwise negative except for bilateral clubbed feet.

Histologic study revealed a superficial zone of necrosis and degeneration on the exposed portions of the myocardium and liver with numerous bacteria on these surfaces. The spleen contained an undue number of polymorphonuclear neutrophils. The remaining organs showed no abnormal changes.

Pathologic Diagnosis.—Congenital malformations were fusion defect of sternum, extrophy of heart, patent ductus arteriosus, coaretation of aorta, hypertrophy and dilatation of heart, omphalocele, and bilateral talipes equinovarus.

SUMMARY

1. A case of ectopia cordis thoracis with associated coaretation of the aorta, patent ductus arteriosus, omphalocele, and bilateral talipes equinovarus is reported.

2. An attempt at surgical repair was unsuccessful.

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CANCER OF THE MALE BREAST TREATED BY ORCHIECTOMY

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THE value of orchiectomy in the treatment of carcinoma of the male breast has been demonstrated in a small number of patients. The purpose of this paper is the presentation of an additional patient with a brief orienting summary of previous literature.

Interest in carcinoma of the male breast has been sporadic because of its comparative rarity—it comprises less than 1 per cent of all mammary cancer. The prognosis is relatively poor for carcinoma of the male breast. Only 3 of 26 patients reported by Gilbert[4] lived for 5 years without signs of recurrence. Wainwright,[14] in a collective review of carcinoma of the male breast, found that the average survival was 33 months after mastectomy, with a 5-year survival of 19 per cent of 111 cases. It should be noted, however, that these were selected cases, many of which were reported for the excellence of the result. Harnett[5] reported a 5-year survival of 4 patients in a consecutive series of 23 men with breast cancer.

Castration or administration of female or male sex hormones for cancer of the female breast has a long history. This has been reviewed by Adair and associates,[1] Nathanson and associates,[11] and Huggins[8] and may be briefly summed up as follows: Surgical or x-ray castration of the female before the menopause may cause marked temporary relief of symptoms and regression of some metastases. The administration of estrogens prior to the menopause seems to accelerate metastatic growth and accordingly seems to be harmful. Before the menopause rather massive doses of androgens may be beneficial. After the menopause and particularly with patients over the age of 60, massive estrogen therapy may be of benefit. Also, androgen therapy may cause a marked temporary improvement, particularly in regard to osseous metastases in this older age group.

Huggins' reports,[6, 7] along with many others, have convincingly demonstrated the value of orchiectomy for carcinoma of the prostate and have given great impetus to the study of the effects of the various endocrine secretions on various types of cancer in the body. Farrow and Adair[3] were the first to report, in 1942, that they had performed a bilateral orchiectomy on a 72-year-old man with osteolytic metastases from primary breast carcinoma. The rapid relief from pain and the roentgenologic evidence of regression led them to treat 12 more cases of male breast cancer in this manner with clinical remission of varying duration in most cases. Treves[13] has recently reported a follow-up analysis of these cases. He has concluded that bilateral orchiectomy has had definite favorable effects upon primary inoperable mammary neoplasms. It had, in varying degrees, promoted healing in remote metastases, notably bone.

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Other isolated cases have been reported. Leucutia,[10] in 1946, described 2 patients, both of whom were over 60 years of age. One with osteolytic metastases had reossification and had survived for over 2 years. The second patient had no bone lesions but developed a diffuse skin recurrence following a radical mastectomy. After castration, he had a 4 month regression of these lesions but died of carcinomatosis after 8 months. Dramatic relief of pain from spinal metastases of a male breast carcinoma was reported 2 months following orchiectomy by Payson and Rosh.[12] Marked regression of pulmonary and osseous growth as well as relief from pain were noted by Karpat and Kuehn[9] in a 60-year-old man. This patient died from overwhelming metastases 2 years following orchiectomy. A 38-year-old Negro with osseous and pulmonary metastases was described by Castillo[2] as having marked relief from dyspnea, pain, and edema following orchiectomy. Contrary to all other cases reported, these metastases were osteoblastic, with a decreased serum alkaline phosphatase. Osteolysis occurred following castration with coincidental increases in the alkaline and acid phosphatases. This patient survived for 21 months following orchiectomy.

CASE REPORT

D. L., a 55-year-old white widowed freight handler, was first seen at Strong Memorial Hospital on Sept. 25, 1947, in the outpatient department, where he was referred for x-ray therapy for metastases of carcinoma of the left breast.

One year previously he had first noted a small lump in the left breast, which gradually increased in size. Six months before, he had noted a lump in the left axilla. Pain in the mid-back and rib cage had begun about 4 months before admission. There had been a 20 pound weight loss in 1 year.

Left radical mastectomy had been performed on Aug. 11, 1947, at another hosptial.

Past history and family history were not contributory.

On examination the patient appeared to be thin, pale, and chronically ill, and weighed 60.3 kilograms. The vital signs were normal. A healing radical mastectomy scar was present on the left chest without any evidence of local recurrence. A small firm lymph node was present in the right axilla. Palpable irregularities and tenderness were present in the lower ribs bilaterally. The liver was tender and extended 4 cm. below the right costal margin. The external genitalia were normal. Rectal examination revealed a smooth, firm prostate of normal size. Vertebral tenderness from the sixth thoracic vertebra to the third lumbar vertebra was marked upon direct palpation.

The blood Wassermann was negative; there was no anemia; the urine sediment contained 5 to 10 red blood cells per high-power field.

Roentgenograms revealed widespread metastatic osteolytic lesions involving the skull, spine, ribs, femurs, and pelvis. The body of the third lumbar vertebra was collapsed. The lungs (Fig. 1) showed moderate parenchymal involvement. The blood calcium and phosphorus were 11.0 and 3.4 mg. per cent, respectively. The alkaline phosphatase was 6.9 Bodansky units or 14.4 King-Armstrong units.

Review of the microscopic sections showed masses, clumps, and columns of atypical cells, some with an acinar arrangement, invading connective, muscular, and lymphoid tissue (Fig. 3). The diagnosis was carcinoma of the male breast with axillary metastases.

Bilateral orchiectomy was performed on Oct. 16, 1947, and the testes were normal, with mature spermia and moderate spermatogenesis present.

The patient was discharged wearing a plaster jacket for support of the collapsed vertebra. On Oct. 30, 1947, the blood calcium was 9.0 mg. per cent, phosphorus was 3.8 mg.

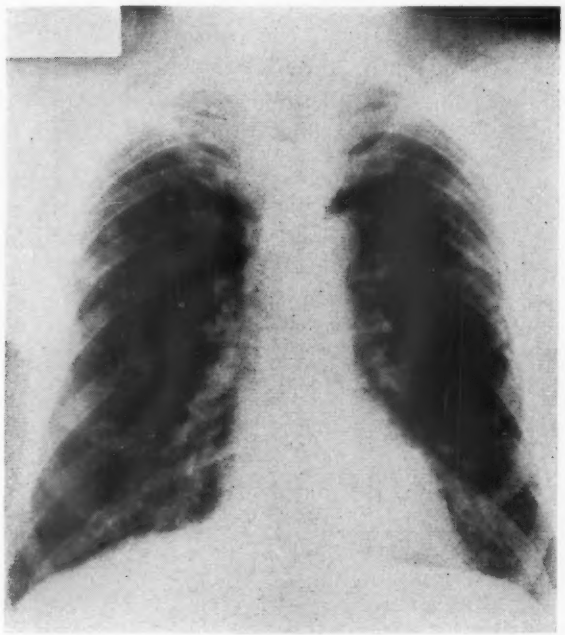

Fig. 1.—Roentgenogram of chest, Sept. 25, 1947. Note the early widespread parenchymal metastases.

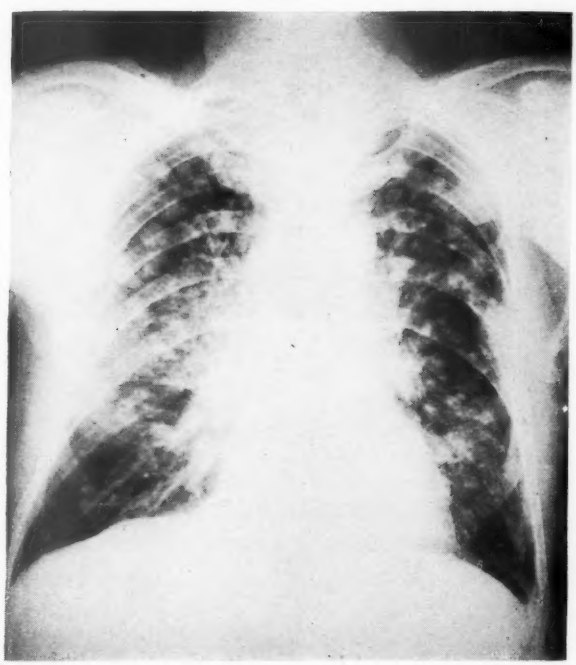

Fig. 2.—Roentgenogram of chest March 29, 1949. Note the marked progression of parenchymal metastases with actual regression of the bony metastasis in the left sixth rib posteriorly.

per cent, and the alkaline phosphatase was 15.4 King-Armstrong units. The body weight was 64.0 kilograms with cast.

Relief from the bone pain was complete within three weeks following orchiectomy. The patient felt well and gained 6 kilograms in 3 months, weighing 70.4 kilograms in January, 1948. However, no changes in the osteolytic processes appeared on repeated x-ray examinations. The alkaline phosphatase was 10.4 King-Armstrong units on Jan. 5, 1948.

The patient continued to be free from pain until March, 1949, 17 months following orchiectomy, when he appeared weaker and began to have return of the bone pain that had been so distressing at the time of the first admission. Alkaline phosphatase was 14.9 King-Armstrong units. He was given 0.005 Gm. stilbestrol 4 times a day without relief of symptoms. The visceral metastases appeared to be extending (Fig. 2). Weight was 59 kilograms with the cast. His condition rapidly became worse, and he died April 12, 1949.

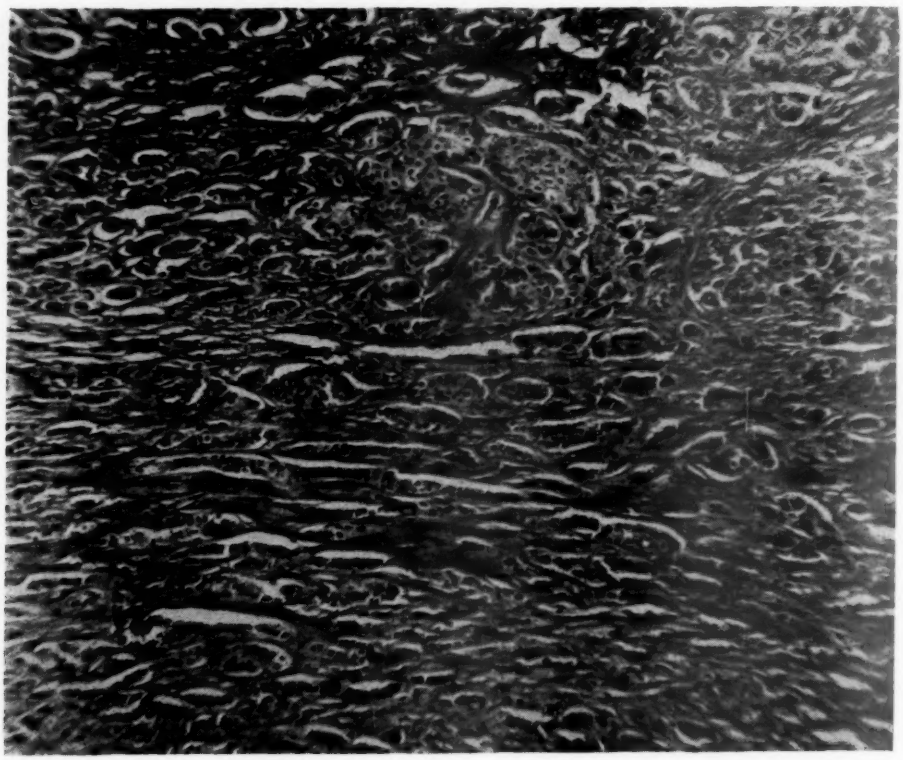

Fig. 3.—Microscopic appearance of breast cancer at the time of radical mastectomy, Aug. 11, 1947.

DISCUSSION

The influence of endocrine secretions on the course of certain cancers is a fascinating phenomenon. The addition or subtraction of male or female sex hormones for a given cancer with benefit therapeutically suggests that the relative hormonal balance may be as important as the specific administration. Beyond a certain point so little is known about the interrelationships of the endocrine glands that most opinions regarding their mode of action on cancer are purely speculative. Certain observations seem important, however. The beneficial effect of endocrine therapy is only transient and does not seem to alter the ultimate prognosis. Second, bony metastases seem to respond more favorably

Fig. 4.—Osteolytic metastases of skull, Oct. 3, 1947.

Fig. 5.—Osteolytic metastases of skull, March 29, 1949, with minimal progression in 18 months.

to androgen therapy and soft tissue metastases seem to respond more favorably to estrogens if they respond at all. Third, the beneficial effect of castration upon metastases from carcinoma of the male breast seems to be as dramatic as from carcinoma of the prostate. It is well known that in the female with breast cancer, before the menopause, the influence of estrogen therapy or pregnancy may be quite disastrous. It is interesting to speculate what the hormonal influence is or has been upon metastatic foci from a carcinoma of the female breast that begins to spread after 20 or 30 years of quiescence. Because of the more complex endocrine pattern in the female, this less predictable response to endocrine therapy may be accepted, if not explained.

Though a radical mastectomy was performed on the patient just presented, he undoubtedly had widespread metastases at the time of operation and his condition was rapidly becoming worse. It is doubtful if he could have lived more than a few months untreated. The dramatic response from castration may be noted in the relief of symptoms, weight gain, and the general subjective sense of well-being. There seemed to be little progression of the bony metastases as noted in Fig. 4 and Fig. 5. Actually, on comparing the first and last chest films, there is regression of some osteolytic lesions, particularly in the left sixth rib. However, there was a marked increase in the soft tissue metastases, which is shown very dramatically in the 2 chest films 2½ years apart. One cannot help but wonder if different malignant components of the same neoplasm are involved, under such circumstances. Our experience with castration and endocrine therapy for cancer of the female breast also suggests that the spread of the soft tissue metastases is the most important terminal event. Of course, the rigid confinement of bony metastases must be considered in evaluating their progression. Unfortunately, post-mortem examination was not obtained, but symptoms and physical and x-ray findings prior to death indicated widespread visceral metastases, intraperitoneally, intrathoracically, and intracranially. Despite the rapid terminal progression of the disease, it should be emphasized that the dramatic relief of symptoms by the simple palliative procedure of orchiectomy made the patient a very effective, comfortable, and happy individual for at least 12 months. It seems important to us to consider these factors in the appraisal of any palliative therapy.

SUMMARY

The case of 55-year-old man with primary carcinoma of the breast treated by orchiectomy is described. Relief from pain was marked. Survival period was 18 months following orchiectomy.

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SIMULATION OF HERNIATED CERVICAL DISC BY THE ARNOLD-CHIARI DEFORMITY

Presentation of Two Cases in Adults

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THE Arnold-Chiari deformity is not uncommon in infancy. Since 1893 when Chiari first noted the anomaly nearly 200 cases in infants have been described in medical literature. We have found but fifteen cases of the condition reported in adults. Presented herewith are two cases of the Arnold-Chiari deformity in adults that represent the sixteenth and seventeenth cases outside of infancy. They are the fifth and sixth cases in which spina bifida has been excluded. To our knowledge no cases have been previously reported where this developmental abnormality of the neural axis has presented history, symptomatology, physical, laboratory, and myelographic findings consistent with the diagnosis of herniation of a cervical intervertebral disc causing radicular compression and radicular pain.

CASE REPORTS

Case 1.—Mrs. E. R. B., a 27-year-old white woman, entered Southern Baptist Hospital on June 3, 1948. Diagnosis of ruptured and herniated cervical intervertebral disc had been made in Dallas, Tex., by an orthopedist, and confirmed by a New Orleans neurosurgeon.

Chief Complaint.—The chief complaint was pain extending from the region of the sixth cervical vertebra to the left suprascapular region, left shoulder, and arm, with numbness and paresthesia of the radial aspect of the left forearm, the thumb, and index finger.

Past History.—The patient had had a normal childhood and early adolescence except that while running in play her head would hurt.

Illness at Time of Admission.—In 1938 cysts were removed from each antrum for the relief of headache, slight exophthalmos, and poor vision. The two latter complaints were relieved, but the headaches persisted. Shortly after the antral operations pain began in the power posterior portion of the neck, left suprascapular region, shoulder, and arm, and persisted to the time of admission. In 1939 she had difficulty in walking. The left leg would cease functioning and simultaneously she would drop any article in the left hand. She had a sudden paralysis of the left side. She was hospitalized at this time and repeated spinal drainage was done for the relief of headache. The paralysis was partially relieved. A ventriculogram done at this time showed a possible blood clot in the right frontal region. There was cramping of the left foot and continuation of headache. Following this the patient was give chiropractic treatments for one year. The leg weakness improved but she had daily headache. The pain in shoulder and arm continued. In 1941, a scalenus anticus section on the left failed to relieve the pain and the headache became more severe. Early in 1948 an acute attack of pain was experienced and the patient was placed under medical care. For the six months prior to admission she had difficulty in walking; hyperextension of the neck caused pain in the neck and left shoulder and slight pain in the right shoulder. Slight incontinence and constipation were present. Pinching of the left forearm caused paresthesia in adjacent areas. The left forefinger, thumb, and radial aspect of the left arm felt like leather. Recently there was soreness in the left third metacarpophalangeal and first phalangeal joints. The patient's condition became worse.

Physical Examination.—Three small cranial defects as created for ventriculography were noted. The cranial nerves functioned normally. Pain followed elevation of the left shoulder against resistance. The left biceps, knee jerks, and angle jerks were hyperactive.

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The left lower extremity was weaker than the right. Paresthesia and impairment of perception of light touch over the radial aspect of the left forearm, wrist, hand, thumb, and index finger were evident (Fig. 1). Definite point tenderness to the left of the midline was noted at the seventh cervical interspace. Limited motion of the neck caused pain in the neck, left suprascapular region, shoulder, and arm. Lumbar puncture revealed an initial pressure of 120 mm. and normal dynamics. The cerebronspinal fluid was clear and colorless. The cell count was 16. Roentgenograms of the skull and cervical, thoracic, and lumbar spine showed no abnormalities or evidence of narrowing of any intervertebral space. Following a cisternal injection of 5 c.c. of Pantopaque a defect at the seventh cervical interspace on the left was observed fluoroscopically (Fig. 2). The radiopaque material fragmented and a satisfactory film was unobtainable. A diagnosis of cervical disc herniation was made and laminectomy was planned.

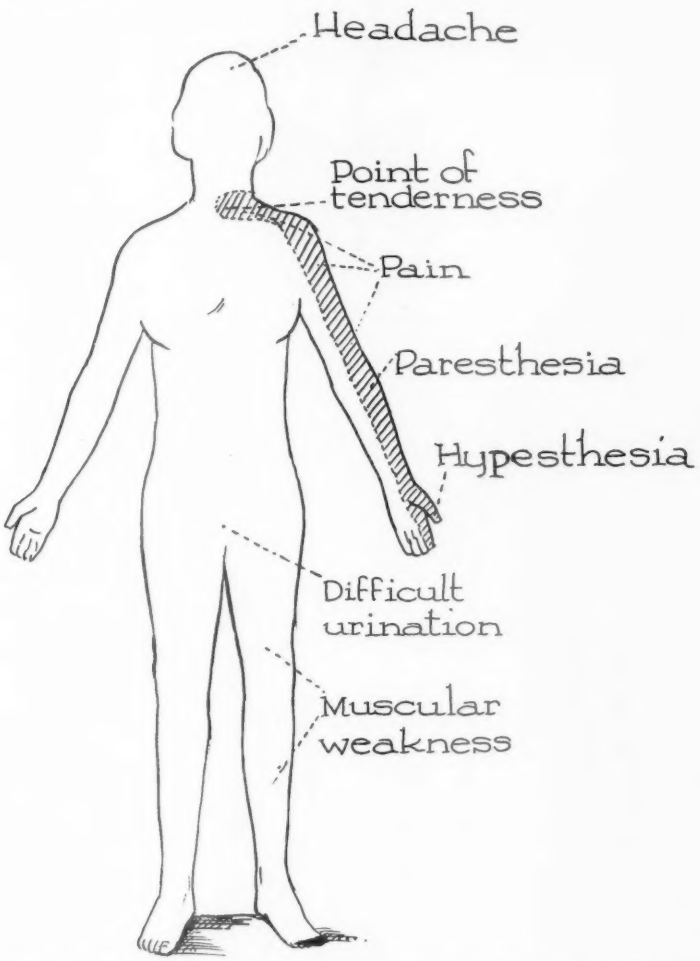

Fig. 1.—Drawing showing symptoms resembling those of cervical disc herniation in Case 1.

Operation.—The laminae and spinous processes of the sixth and seventh cervical and first thoracic vertebrae were removed. The dural sac appeared normal. Excision of bone was carried out into the left seventh intervertebral foramen. The nerve left the dural sac with angulation reversed. This finding suggested disc herniation (Fig. 3, *A*). Thorough exploration failed to reveal one. The same structural anomaly was revealed upon exposure at the sixth cervical and first thoracic vertebrae. Exposure of the sixth and seventh cervical and first thoracic intervertebral foramina showed a like reversal of the normal angulation (Fig. 3, *B*).

The diagnosis was then obvious. A complete cervical laminectomy was done, and an adequate subtotal occipital craniectomy accomplished. The atlas was invaginated into the foramen magnum, although there was no radiographic evidence of platybasia. A very large and tortuous artery was seen on the left at the foramen magnum. Opening of the dura from the superior limit of its exposure to the level of the fifth cervical vertebra showed a few

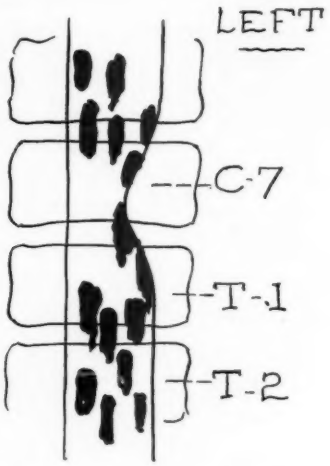

Fig. 2.—Filling defect observed fluoroscopically after injection of Pantopaque into cisterna magna in Case 1. A similar defect was observed in Case 2 on the right side.

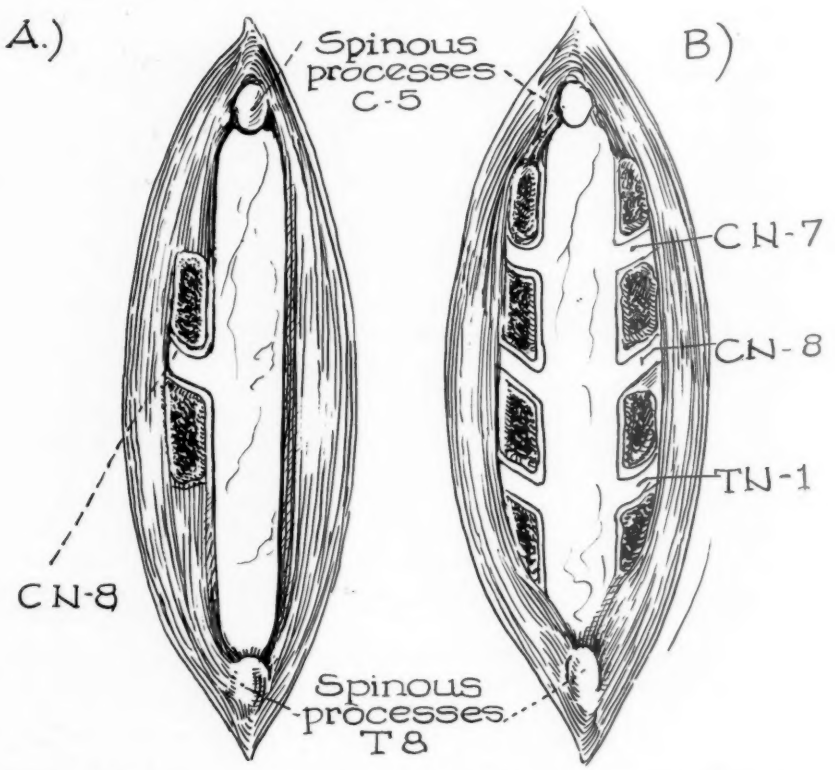

Fig. 3.—*A*, showing exposure of dural sac and the eighth cervical nerve leaving the dural sac, with reversal of the normal angulation; *B*, showing the seventh and eighth cervical and first thoracic nerves exposed bilaterally, all displaying reversal of angulation.

fine adhesions of the leptomeninges and the usual tongue of cerebellar tissue. The caudal portion of the cerebellum, fourth ventricle, and medulla occupied the foramen magnum and upper portion of the cervical spinal canal. The junction of medulla and cord was at the level of the third cervical vertebra. The dura was left open and closure accomplished.

Postoperative Course.—This patient complained of pain in the right shoulder, suprascapular, and supraclavicular regions, hyperesthesia of the left breast, anesthesia of the radial aspect of the left forearm, wrist, thumb, and index finger, and loss of proprioceptive sense at various times. She was discharged from the hospital on the eighteenth postoperative day. Later complaints were many and varied, the most persistent and severe of which was pain in the right buttock, hip, posterior portion of the thigh, calf, and foot. It was thought that possibly adhesions of the nerves of the cauda equina to the dura and overlying structures were responsible. Lumbar laminectomy on Nov. 22, 1948 failed to reveal any abnormality of the spinal canal or cauda equina. Hoping to relieve the then persistent complaints of headache, head noises, and hyperesthesia of the scalp, operation was carried out on Feb. 17,

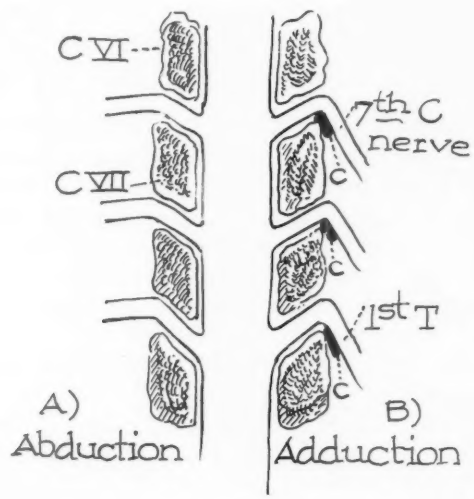

Fig. 4.—Diagram showing my conception of how the second patient could increase his pain by holding the right upper extremity to the side, and decrease pain by elevating and abducting the extremity.

1949, with enlargement of the occipital craniectomy to the maximum. No adhesions were noted, the dura remained open, and there was free circulation of cerebrospinal fluid. The large artery seen at the first operation was no longer evident. Some symptoms persist although no anatomic basis for any of the postoperative complaints have been found. A neuropsychiatrist has diagnosed the patient's condition as hysteria. On May 21, 1949, the patient was doing her cooking and housework and leading a normal life, although she still complained of pain in the left lower extremity, headache, and occasionally a feeling of fainting.

Case 2.—N. T., a 31-year-old white man, was admitted to the Charity Hospital of Louisiana on Aug. 11, 1948.

Chief Complaint.—The chief complaint was pain near the base of the neck posteriorly, in the region of the right trapezius muscle, and down the right arm to the index finger, middle finger, and thumb.

Illness at Time of Admission.—Ten weeks before admission, about June 1, 1948, the patient experienced a sudden stabbing pain in the right side of the neck, along the trapezius muscle, and down the right arm and forearm to the right index and middle fingers and right thumb, where the pain was most severe. There was cramplike pain in the forearm which was

increased by coughing and sneezing. It was relieved somewhat by elevation and abduction of the right upper extremity, and increased by lowering and adducting to the side of the body (Fig. 4). Numbness accompanied the pain. There had been treatment in the orthopedics clinic from July 2, 1948, and he had received one stellate block without relief. When the patient was brought to neurosurgery the tentative diagnosis was herniated cervical disc.

Physical Examination.—There was tenderness on deep palpation over the sixth and seventh cervical interspaces and superior to the spine of the right scapula. Hyperextension of the neck and turning the head to the left were painful. Pressure over the seventh cervical interspace caused pain in the right trapezius, radial aspect of the right forearm, thumb, and index finger. There was diminished perception of painful stimuli and touch over the entire right arm, most marked over the radial aspect of the forearm, thumb, and index finger. Lumbar puncture revealed normal pressure and dynamics. The cerebrospinal fluid protein was 43.8. A myelogram following cisternal Pantopaque instillation, 3 c.c., was unsatisfactory. It descended to the lower cervical region where it trickled drop by drop past an apparent obstruction on the right at the level of the seventh cervical intervertebral disc. An additional injection of like amount produced the same result. Again, satisfactory films could not be obtained. Laminectomy was decided upon, with the preoperative diagnosis of herniated seventh cervical disc.

Operation.—Laminectomy was performed on the fifth, sixth, and seventh cervical and the first thoracic vertebrae. At the site of the myelographic defect the eighth cervical nerve was exposed on the right at the seventh cervical interspace. It left the dural sac at an acute angle, reversal of the normal anatomy. No disc herniation could be found and experience with Case 1 provided reason for suspecting an Arnold-Chiari deformity. The right seventh cervical and first thoracic nerves were uncovered with the same result. The left seventh cervical nerve was then exposed and reversed angulation revealed. It was hoped that the patient's symptoms would be relieved by this conservative procedure and the wound was closed. Shortly after surgery the patient became cyanotic for five minutes but there were no neurological symptoms.

Postoperative Course.—On the third day after operation pain was relieved and on Aug. 23, 1948, the pain had almost entirely disappeared, although numbness continued in the radial portion of the right forearm, thumb, and index finger. Twelve days after surgery the patient reported that he felt well, and on Sept. 15, 1948, one month after operation, he had returned to work. When last seen, May 16, 1949, there were no symptoms except a slight degree of pain in the left scapular region.

DISCUSSION

The pathologic anatomy of this deformity has been well worked out and established by the work of Campbell,[4] Lichtenstein,[9, 10] and Wagner.[18] Spina bifida and adhesions of nerves and cord are not necessary for the production of the Arnold-Chiari anomaly, as shown by the cases of Bucy and Lichtenstein,[3] Chorobski and Stepien,[5] Swanson and Fincher,[17] and my two cases. A double angulation of the upper spinal nerves has been demonstrated by Campbell,[4] the first occurring as they leave the cord, the second as they exit from the intervertebral foramina. In my opinion this seems especially true in the cervical region, particularly when the upper extremity is held dependent at the side of the body. I also believe that this second angulation may cause symptoms simulating radicular compression by a herniated cervical disc. This is borne out by the fact that the second patient could relieve pain by abducting and elevating the right upper extremity, and increase pain by holding the extremity to his side (Fig. 4).

Concerning the preoperative diagnosis, one should be aware of the possibility of the presence of the Arnold-Chiari deformity when symptoms of herniated cervical disc are presented, especially in the absence of a history of trauma. The histories of my cases were atypical in this respect. The discovery of an atypical filling defect at the appropriate level should be discounted as far as cervical disc is concerned unless actual deformity of the dural sac can be demonstrated fluoroscopically and on the x-ray films. I believe that the atypical filling defect should be taken as possible evidence of the existence of the Arnold-Chiari deformity. In all cases where the previously mentioned conditions exist, the method of Adams, Shatzki, and Scoville,[1] or that of Marks and Livingston,[11] should be resorted to in an effort to demonstrate the deformity preoperatively.

Liable to be confused with the Arnold-Chiari deformity when it simulates cervical disc herniation are cervical disc herniation itself, tumor of the cervical cord, arthritis of the spine, and chronic hypertrophic spinal pachymeningitis. The neurologist or neurosurgeon should have little difficulty differentiating cervical cord tumor. Arthritis would possibly be manifest elsewhere and demonstrated by radiographs. Chronic hypertrophic spinal pachymeningitis as discussed by Colclough, Greenberg, and Jones,[6] probably offers the greatest stumbling block. It may be differentiated in that pain of radicular type is usually bilateral, a history of an infectious process is elicited, and percussion tenderness is found to be more acute.

SUMMARY

1. The occurrence of the Arnold-Chiari deformity in the adult is reviewed.

2. The sixteenth and seventeenth reported cases of the anomaly outside of infancy are presented.

3. The first and second cases of the occurrence of the deformity simulating herniated cervical disc are recorded.

4. Briefly considered are the preoperative and differential diagnoses of the Arnold-Chiari malformation simulating herniation of a cervical intervertebral disc.

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LEIOMYOMAS OF THE ESOPHAGUS

A Report of Five Cases

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THIS is a report of 5 cases of leiomyoma of the esophagus. Four cases were not diagnosed clinically, and with one exception there was no symptomatic history of the presence of leiomyomas until they were found incidentally at autopsy. They were wholly unrelated to the disease from which the patient died. The fifth patient, who had vague clinical symptoms relative to the gastrointestinal tract, was operated upon for partial obstruction of the lower end of the esophagus. The obstruction to the esophagus had been originally discovered by x-ray examination and confirmed by esophagoscopy previous to operation.

Adams and Hoover,[1] reporting 3 cases of benign tumor of the esophagus, gave in addition a comprehensive review of the literature on the subject. They quoted Patterson, who could find only 62 cases reported between 1712 and 1932, many of which were incidental autopsy findings. These authors were able to report 26 additional cases from 1933 to 1943 and with their own 3 cases gave a total of 91. Of all these cases only 6 were reported as leiomyoma.

On the other hand, Calmenson and Clagett,[2] in reporting a case of leiomyoma of the esophagus, said that in a series of 7,459 post mortem examinations performed at the Mayo Clinic, 32 of 44 benign tumors found in the esophagus were leiomyomas. Further reading of the literature since 1943 shows a few more case reports. Kensworthy and Welch[3] reported a leiomyoma involving esophagus and cardia of the stomach which had ulcerated and was resected. They reported only 5 such cases in all literature.

From these reports there seems to be some discrepancy in the proportion of leiomyomas to the total number of all kinds of benign tumors of the esophagus as reported by different authors.

In general, benign tumors of the esophagus may be divided into 2 groups on the basis of their site of origin. One group comprises those tumors arising from the mucosa and submucosa; they are intraluminal and are covered with mucosa. They may be pedunculated and may cause symptoms by their presence in the lumen of the esophagus. The other group is intramural, arising from the outer layers of the esophagus, and these tumors may cause symptoms by extrinsic pressure on the lumen of the organ. Leiomyomas are in this latter class.

CASE REPORTS

All cases were observed within the period of 1 year.

Case 1.—A. K. (47-11), a 72-year-old white man, had a long history of coronary artery and heart disease, as well as hereditary hemorrhagic telangiectasia (Rendu-Osler-Weber disease). He had had some history of difficulty in swallowing of 1 year's duration. At autopsy, 2 well-circumscribed masses, well encapsulated, attached to the outer wall of the esophagus at its lowest portion were seen. The masses were easily shelled out. The larger mass measured 4.5 cm. in diameter. The smaller mass measured 3.0 cm. in its greatest width. The esophageal

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mucosa in the region of the tumor masses was extensively eroded. The masses on cut surface presented a pearl-white color. Histologically the tissue was composed of smooth muscle fibers in whorl configuration, not unlike that seen in uterine fibroids. (See Fig. 1.)

Fig. 1.

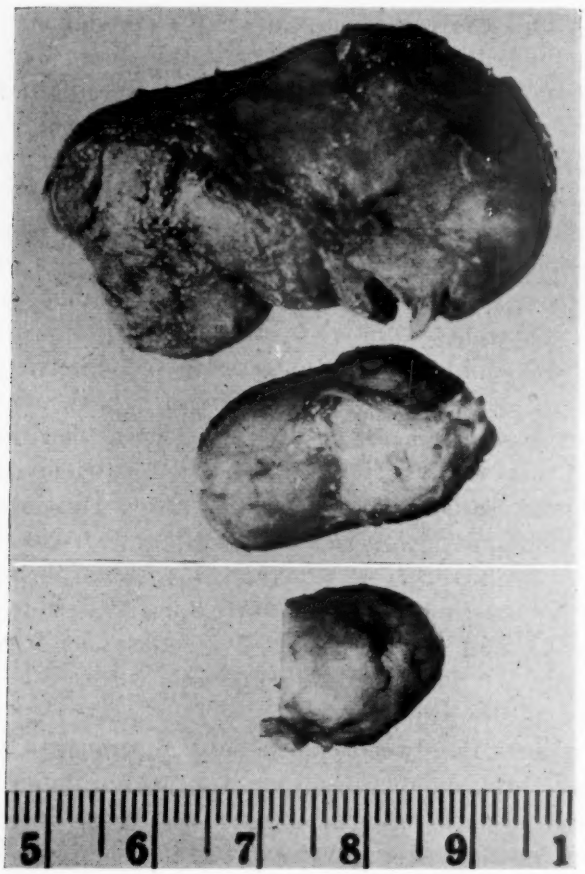

Fig. 2.

Fig. 1 (Case 1).—Photograph of the 2 tumor masses seen at the lower end of the esophagus.
Fig. 2 (Case 2).—Photograph of the small mass seen at the lowest portion of the esophagus.

CASE 2.—R. P. (47-22) was a 69-year-old white man who died of a right cerebral hemorrhage. Autopsy revealed a firm, well-encapsulated mass of rubbery consistency at the lowest end of the esophagus. The mass was present in the outer wall of the esophagus and measured 2.0 cm. in its greatest diameter. Histologically, the mass was composed of large, smooth muscle bundles in whorl configuration. (See Fig. 2.)

CASE 3.—J. R. (48-8) was a 61-year-old white man who died of a massive right cerebral hemorrhage. Autopsy revealed the incidental finding of a small, easily shelled out, pea-sized mass in the posterior wall of the lower end of the esophagus. The mass was found 4.0 cm. above the cardia. The mass had a rubbery consistency and histologically presented the characteristic features of leiomyoma. (See Figs. 3 and 4.)

CASE 4.—W. K. (48-47) was a 62-year-old white man who died of a right cerebral thrombosis. Autopsy showed a small firm white mass measuring 1.5 cm. in its greatest diameter, noted in the anterior wall of the esophagus in its lower segment.

CASE 5.—A. R. (No. 150329), a 54-year-old woman, was admitted Oct. 14, 1947, and discharged Nov. 13, 1947.

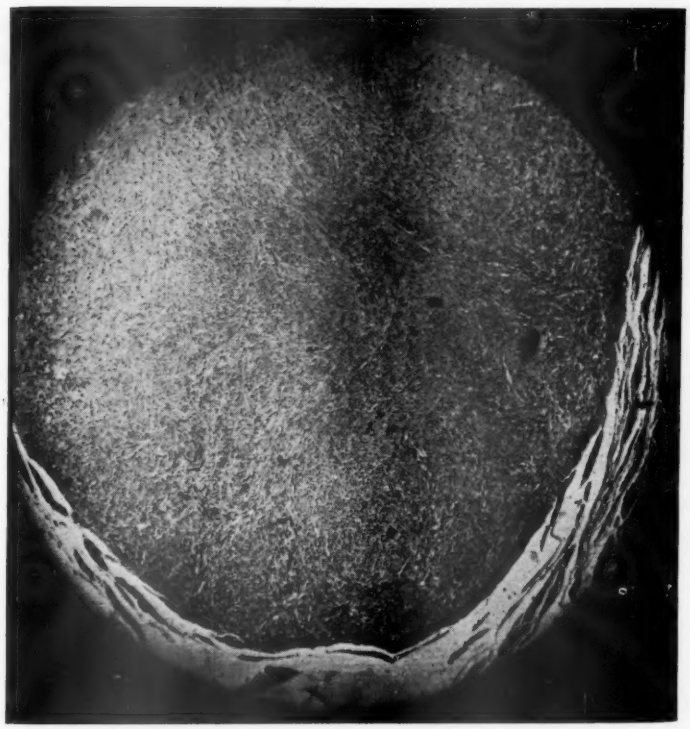

Fig. 3 (Case 3).—Low power photomicrograph illustrating the loose encapsulation of the tumor mass.

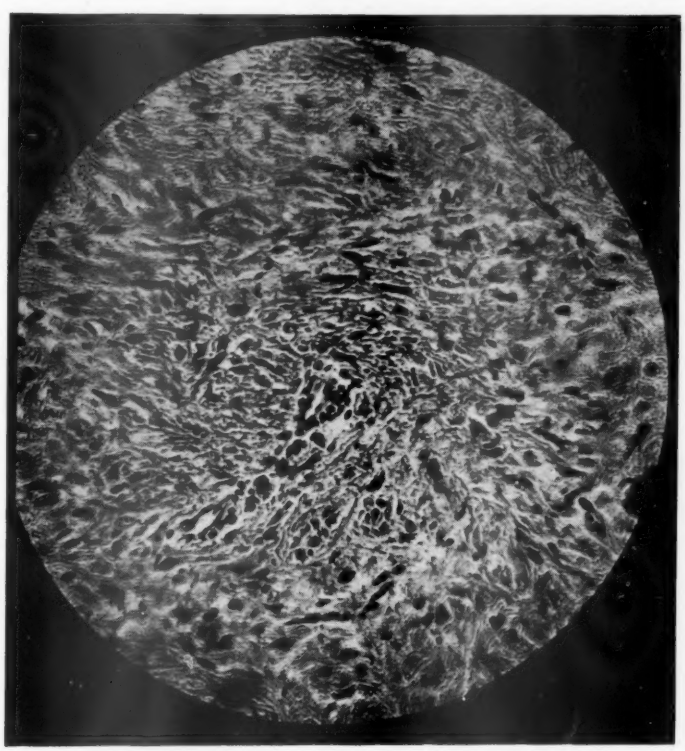

Fig. 4 (Case 3).—High power photomicrograph illustrating the characteristic histology.

Chief Complaints.—She complained of occasional attacks of nausea, "gas pains," and pain in the right scapula. She was unable to eat sweets, fried food, or anything sour. When she had an upset stomach she was relieved by taking soda bicarbonate.

Past History.—Seven years before admission she was operated upon at another hospital for a tumor that "grew outside the uterus." Radium was applied for 24 hours in order to stop menstruation. While in that hospital she had a gall bladder attack. X-ray films revealed large stones, but she refused operation at that time. She had an appendectomy 18 years ago.

Physical Examination.—The patient was a rather obese white woman who did not look acutely, nor chronically, ill. Blood pressure was 106/70. Heart and lungs were negative. Examination of the abdomen revealed no tenderness and no palpable masses. The remainder of the examination was negative.

Laboratory Findings.—The complete blood count was: hemoglobin 76 per cent, 11.05 Gm.; red blood cell count 3,600,000; white blood cell count 7,600; polymorphonuclears 59 per cent; lymphocytes 38 per cent; monocytes 3 per cent; and platelets adequate. Urine was negative. Blood sugar was 90 mg. per cent; nonprotein nitrogen 30 mg. per cent; chlorides 495 mg. per cent; and prothrombin time 21 seconds (Quick method).

TABLE I. GASTRIC ANALYSIS

FASTING	FREE HCl (DEGREES)	TOTAL (DEGREES)
1	0	8
2	26	32
3	10	16
4	14	24
5	10	18
6	0	2
7	12	22

X-ray Findings.—The gall bladder was filled with opaque dye and gave no evidence of nonopaque or opaque calculi; however, it delayed in emptying. In the gastrointestinal series, barium taken by mouth passed through the esophagus without obstruction. The proximal two-thirds appeared normal. There was a constant defect of the left posterior aspect of the esophagus. The adjacent mucosa was irregular. The defect was 3 to 4 cm. in length and about 5 cm. above the cardia. The stomach and duodenum were free of defect. Barium enema showed multiple diverticula of the colon, most numerous in the lower descending and pelvic colon. Diagnosis was defect in lower esophagus consistent with neoplastic disease without obstruction. Esophagoscopy was strongly recommended. (See Fig. 5.)

Esophagoscopy.*—Under Forrestier's solution as a local anesthetic the upper esophagus was exposed with 22 cm. Roberts esophageal speculum. No pathologic changes were noted. The 9 by 45 cm. esophagoscope was passed and at about 36 cm. from the upper teeth there was noted fixation and rigidity of the esophageal wall. At this point a hard, fixed, firm mass was encountered so that the scope was not able to pass beyond this mass. This apparently was extrinsic and encroaching upon the esophageal lumen. At no point was there noted pathologic tissue for biopsy and therefore neither biopsy nor Papanicolaou stains were made.

Operation.—Under sodium pentothal, cyclopropane, and ether anesthesia, an endotracheal tube was inserted. The patient was placed on her right side on the operating table and the left chest painted with two coats of tincture of Merthiolate. The seventh intercostal space was selected and an incision made beginning just to the left of the sternum, extending back to the spine, and then curving upward over the fifth, sixth, and seventh ribs. These ribs were cut across near the spine and the chest cavity opened. The esophagus was seen and near its lower end a lobulated tumor 7 by 4 by 4 cm. was found attached to its anterior and left lateral wall. (See Fig. 6.) Muscle fibers of the esophagus ran into the tumor. One of us (J. G. S.) was consulted at this time and he expressed the opinion that the tumor was a benign myoma. The diaphragm was split and the stomach

*By Dr. P. Latella.

and gall bladder were palpated through the diaphragm; no pathologic changes were found in either. The lower end of the esophagus was freed with the cardiac end of the stomach and no further pathologic changes could be found. The tumor was dissected from the wall of the esophagus leaving the mucous membrane intact. The large defect in the muscular coat of the esophagus was closed by interrupted sutures of fine silk. The diaphragm was closed with interrupted sutures of silk. The chest cavity was thoroughly aspirated of all blood, the left lung was re-expanded, and the chest closed using heavy silk sutures around the sixth and seventh ribs. The muscles were closed with interrupted fine silk sutures, and the skin closed with interrupted silk. No drains were used. The immediate postoperative condition was good. A Levine tube was inserted intra-orally for Wangensteen drainage.

Fig. 5 (Case 5).—Right oblique view showing filling defect with no obstruction to passage of barium through the lower end of the esophagus.

Pathologic Report.—The gross specimen consisted of a well-encapsulated, irregular, nodular mass which measured 7 by 4 by 4 cm. The mass had a firm, rubbery consistence. On section the cut surface revealed tissue of pale brown color and fleshy appearance. A coarse whorl configuration was noted. Microscopic sections examined revealed tissue composed of large irregular bundles of somewhat atypical smooth muscle fibers in whorl configuration. The tissue was relatively acellular. The diagnosis was leiomyoma.

The patient's convalescence was uneventful and she was discharged on the thirtieth postoperative day. She developed a hiatal diaphragmatic hernia diagnosed after discharge. This was repaired 1 year later. She is now in excellent health.

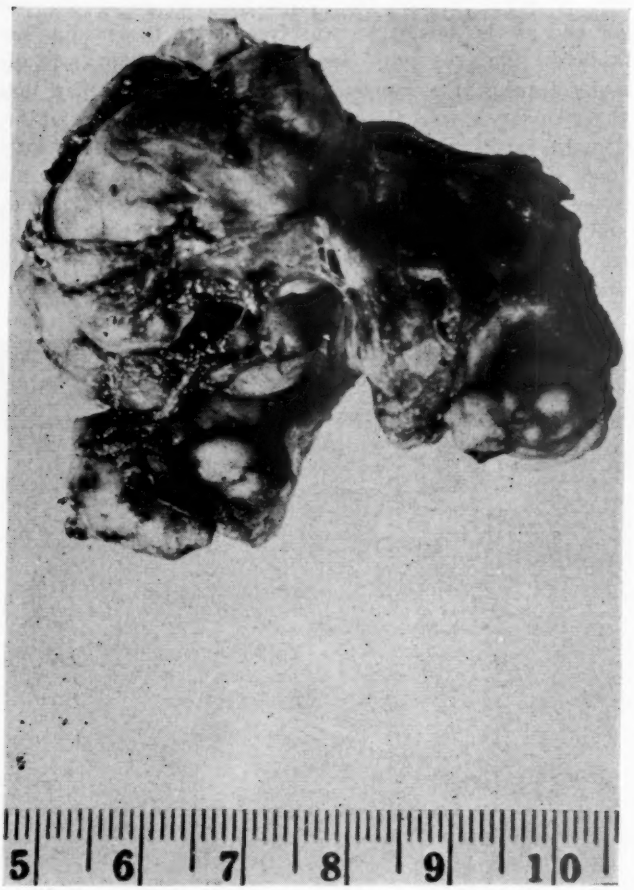

Fig. 6 (Case 5).—Photograph of tumor mass removed operatively.

DISCUSSION

A review of the literature and 5 additional cases of leiomyoma of the esophagus are reported. Four of these cases were incidental autopsy findings and 1 case was operated upon for partial esophageal obstruction.

From an exhaustive review of the literature by various authors it can be concluded that reported benign tumors of the esophagus are rare as compared to malignant tumors. Leiomyomas comprise a small but variable number of these tumors. They manifest few clinical symptoms, and most cases are found incidentally at autopsy. The treatment when they cause symptoms during life is surgical removal. All of the leiomyomas can be removed without resection of the esophagus. No case of malignant degeneration of this tumor has been reported. The chief reason for surgical intervention is obstruction.

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CARCINOMA SECONDARY TO BURN OF THE ESOPHAGUS FROM INGESTION OF LYE

Report of a Case

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(From the Medical College of Virginia)

IN SPITE of efforts to restrict the sale of lye for household purposes, accidental and suicidal ingestion of this substance still remains one of the frequent causes of benign stricture of the esophagus. When lye is taken with suicidal intent, death usually results from extensive destruction of the esophagus and stomach. When only a small quantity is ingested, the resulting burns are followed by cicatricial contraction and reduction in the lumen of the esophagus. The strictures thus produced require many months of treatment before healing occurs and normal deglutition is restored.

A complication that is usually not anticipated following ingestion of lye is the development of malignant degeneration in the scar of the burn. Of approximately 200 patients with such burns of the esophagus we have seen carcinoma develop at the site of the stricture in seven. As the majority of the patients whom we have observed with burns from ingestion of lye have been children less than 5 years of age, carcinoma may develop in other members of this group of 200 patients within the next few decades.

Another fact of interest is that we have not observed malignant degeneration in the scars of benign strictures from other causes.

REPORT OF CASE

The most recent patient in whom carcinoma developed in our group of cases of stricture following ingestion of lye was a woman 47 years of age who accidentally swallowed a solution of lye when she was 4 years old. She does not remember whether or not treatment was given at the time of the accident, but she had varying degrees of dysphagia thereafter.

On several occasions the esophagus was completely obstructed for one day or more at a time. When she was 7 or 8 years old, she was unable to swallow anything for approximately two weeks, but this period of obstruction was relieved when she regurgitated a plum stone which had, according to the patient, sprouted in the esophagus. The degree of dysphagia remained about the same for many years, and she drank much water with her meals to assist her in forcing food through the esophageal stricture into the stomach.

About July, 1948, dysphagia became more noticeable without apparent cause, and in May, 1949, the stricture was dilated. A week later esophagoscopic examination was made, following which empyema developed on the right side and required surgical drainage. Food was not identified in the material evacuated from the thorax. By the early part of July, 1949, the patient had recovered from the empyema, but the dysphagia became more severe.

We saw the patient for the first time on Oct. 4, 1949, when she was able to swallow liquids only, and these had to be taken very slowly and in small amounts. The presence

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of carcinoma in the scar of the burn from the lye was suspected, but roentgenoscopic study using Lipiodol as a contrast medium revealed a smooth outline at the site of the stricture (Fig. 1).

On Oct. 6, 1949, a No. 29 French sound was passed over a guiding thread through the stricture, which was located 9 inches from the incisor teeth. The chief point of obstruction to passage of the sound was about 3 cm. below the upper end of the stricture, and a small amount of bloody mucus was noted on the dilator when it was withdrawn from the esophagus.

Fig. 1.—Roentgenogram of esophagus showing a smooth outline at site of stricture.

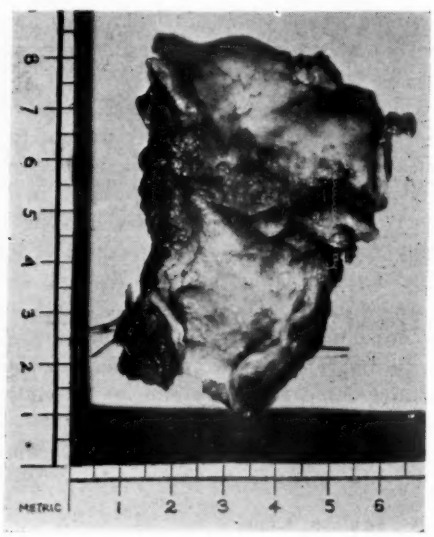

Fig. 2.—Gross surgical specimen of esophageal carcinoma.

Swallowing was not improved following dilation, and the following day esophagoscopic investigation was performed under intravenous anesthesia. Esophagoscopic study revealed narrowing of the upper portion of the esophagus and, in the depths of the stricture, an area of infiltration that resembled carcinoma. Tissue removed for microscopic examination was diagnosed as squamous-cell carcinoma, grade 3.

The following day the esophageal lesion was removed surgically (Fig. 2), and at the time of the writing of this report (two weeks postoperatively) the patient was convalescing satisfactorily. There was no evidence of extension of the growth outside the lumen of the esophagus, although the tissues at the site of the tumor were densely adherent as the result of previous infection.

HEMORRHAGE INTO THE FALCIFORM LIGAMENT OF THE LIVER AS A CAUSE OF ACUTE ABDOMINAL SYMPTOMS

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SPONTANEOUS hemorrhage into the falciform ligament of the liver as a cause of acute abdominal symptoms has, to our knowledge, been described only once. In 1931, Lambert[1] reported the case of a 46-year-old carpenter, who, without a history of immediately antecedent trauma, suddenly developed epigastric pain and nausea. Physical examination disclosed generalized abdominal spasticity and tenderness, most marked in the epigastrium. The preoperative diagnosis was that of perforated peptic ulcer, and the patient was subjected to laparotomy. The falciform ligament was found to be redundant, and in the central portion there was a localized area of hemorrhage, dark purplish-red in color. Further abdominal exploration revealed a dilatation of the stomach but no other intraperitoneal abnormality. The falciform ligament was resected and an uneventful recovery resulted.

Mention is made by Reimann and Cowley[2] of ruptured varices of round ligament as a cause of intra-abdominal hemorrhage, but no case report or reference is cited.

CASE REPORT

M. A. K. (Chart No. 37542), a 30-year-old white man, was admitted to the Middlesex General Hospital on Feb. 3, 1949. Three days before admission he lifted a heavy box, and within an hour of this exertion he noticed the gradual appearance of pain in the right upper quadrant of the abdomen. The pain was dull and steady in nature and did not radiate. After achieving its peak intensity on the first day, it persisted unchanged to the time of hospitalization. Nausea and anorexia were present in the first twenty-four hours only. There was no emesis. The patient stated that he felt most comfortable lying still in bed with the knees in moderate flexion. Motion aggravated the pain. His past history included mild transient episodes of pain in the right lower abdomen over the past year. There was no history of belching or fatty food intolerance.

Examination revealed an adult male in only mild distress from abdominal pain. Temperature was 98° F. Physical examination except for the abdomen revealed findings within normal limits. The blood pressure was 120/80. The abdomen was not distended. Splinting of the abdominal wall in the upper right quadrant was noted. Localized tenderness was present one and one-half inches below the right costal margin at the lateral border of the rectus muscle. Neither rebound tenderness nor shock tenderness could be elicited. Rectal examination revealed no tenderness.

Urinalysis was negative. The white blood cell count was 6,100 with 58 per cent polymorphonuclear leucocytes and otherwise normal differential count. The red blood cell count was 4,940,000 per c.mm., with a hemoglobin of 15.7 Gm.

The diagnosis on admission was acute cholecystitis. The more remote possibility of an atypical acute appendicitis was also considered. The patient entered the hospital in the late afternoon and was given tablets of Priodax (iodoalphionic acid) preparatory to x-ray study of the gall bladder, which was performed early the next morning. A normally filling viscus containing no stones was visualized. Laparotomy was carried out some nineteen hours after admission.

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Operation.—Under cyclopropane-ether anesthesia the abdomen was entered through a right rectus muscle-splitting incision whose mid-point was at the level of the umbilicus. There was no free fluid in the peritoneal cavity. The appendix was found to be normal. Further examination revealed an inflammatory mass approximately 2.5 cm. in diameter in the region of the lower falciform ligament. This was loosely adherent to the anterior surface of the transverse colon and to the near-by greater omentum by loose fibrinous adhesions easily separated with the finger. When thus partially freed, the mass appeared dark purplish-red in color, and had the appearance of a hemorrhagic and partially necrotic mass of fat tissue

Fig. 1.—Area of hemorrhage into the fat tissue as seen from the serosal aspect (left) and the cut surface (right). The mass at operation was approximately twice as large as illustrated. (Photograph taken after formalin fixation and subsequent to removal of tissue for microscopic examination.)

originating by a broad base from the falciform ligament and anterior abdominal wall. No evidence of torsion was present. Immediately below the lesion was another fat lobule of almost similar size, constituting the extreme lower portion of the falciform ligament. At this site the fatty tissue appeared grossly normal. The hemorrhagic mass was cut away from the anterior abdominal wall and removed. The rent in the parietal peritoneum was repaired with interrupted cotton sutures. Appendectomy was carried out prior to the closure of the abdomen in layers.

*Pathologic Examination.**—The specimen consisted of a resected ovoid, rounded, firm mass of fat tissue, measuring 2.8 by 1.5 by 1.0 cm. It was indurated and dark purplish-red

*By Dr. Sylvan E. Moolten.

in color over a large portion of its substance. On section, the indurated portion appeared to be composed almost wholly of hemorrhagic fat tissue. In addition, a separate mass of fat the size of a filbert was present and showed no remarkable features (Fig. 1).

Sections through the indurated mass of fat revealed massive hemorrhagic infiltration extending between and within the lobules, separating many of the individual fat cells and apparently causing their necrosis. The cause of the hemorrhage was not apparent. The necrosis within the affected area appeared to be secondary to hemorrhage and there was only minimal focal infiltration of leucocytes. The serosal aspect of the hemorrhagic area was covered by fibrinous exudate, which showed beginning organization into a compact lamina.

Pathologic Diagnosis.—Diagnosis was fat tissue of the peritoneum showing recent hemorrhagic infiltration with secondary necrosis and beginning reactive inflammation and fibrosis.

The patient's postoperative course was uncomplicated. Ambulation was begun on the third day after surgery, and he was discharged from the hospital three days later. At follow-up examination five months after surgery the patient was found to be asymptomatic.

DISCUSSION

The main clinical features of this case deserve special emphasis: (1) the age and sex of the patient; (2) the preceding violent exertion, calling for tensing of the rectus abdominis muscles and coincident increase in venous pressure due to straining; (3) the gradual progressive onset of symptoms shortly after the exertion; (4) the localization of pain and tenderness to the right upper abdomen; (5) the lack of appreciable systemic or reflex visceral symptoms; and (6) the absence of hypertension or blood dyscrasia.

It is likely, because of the fixed position of the falciform ligament, that the symptoms and signs in any subsequently occurring case would be quite similar. This is in contrast to the clinical syndrome produced by the twisted appendix epiploica, where the lesion may occur almost anywhere along the colon. It warrants consideration in patients with right upper quadrant symptoms where gall bladder and other intra-abdominal pathology can be ruled out, although the rarity of the condition may preclude its preoperative recognition.

SUMMARY

A case of spontaneous hemorrhage into the fat tissue of the lower falciform ligament is presented, and the clinical features are elaborated.

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TRAUMATIC RUPTURE OF THE AORTA

Report of a Case in Which the Patient Survived for Eighty-One Days

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OF NINETY cases of traumatic rupture of the aorta reviewed in the available literature, there were 64 deaths occurring within 1 hour following the injury. Only 7 patients survived for more than 18 hours. Of these, 5 had tears just above the aortic cusps, with hemorrhage into the pericardial sac. Kuhn[12] reported a case in which the patient lived 10 days following rupture of the aorta. In this particular instance the rupture was located in the first part of the aorta, the patient dying as a result of cardiac tamponade. Blalock,[1] Elkin,[7] and Dshanelidze[6] each reported successful closure of the defect in a case of rupture of the aorta with bleeding into the pericardial sac. Closure of the rupture apparently has not been accomplished in cases in which the rupture occurred outside the pericardial sac, which is doubtless due to the fact that the patient dies almost immediately following the injury. The diagnosis of rupture of the aorta often is masked by more or less severe concomitant injuries.[15, 17] While the cases reviewed indicated that the injuries for the most part were the results of automobile accidents, more pedestrians than passengers were injured. In some of the cases, the injuries resulted from falls, or jumps from a height, or followed a blunt force to the thorax.[8, 10] There were 4 cases[1, 6, 7] of stab wounds of the chest, and 1 case of bullet wounds[14] of the same area. Only 9 cases were reported in which there were no fractures involving the chest,[2, 4, 5, 8, 9, 15, 18] that is, ribs, sternum, or vertebrae, or a combination of these. In most cases, death was caused by shock due to severe blood loss. There was hemorrhage either into the mediastinum and left chest cavity, or into both chest cavities. In none of the cases reported was the hemorrhage confined entirely to the right chest and mediastinum as was true in our case.

The most common site of the rupture was below the origin of the left subclavian artery at the insertion of the ligamentum arteriosum,[3, 5, 9, 11, 15, 16] this being true in 47 of the 90 cases reviewed. There were 20 cases of rupture of the ascending aorta,[13] 17 of the descending aorta, and 3 of the abdominal aorta. In 12 cases the rupture occurred in more than 1 place. In 8 cases[15] the rupture was incomplete, the adventitia being intact but dissected away from the intima by hemorrhage.

The mechanism of rupture of the aorta is not known. Some observers[11, 16] believed that rupture at the insertion of the ligamentum arteriosum is more common because the aorta is relatively fixed at that point, while in its descent it is relatively mobile, and thus that the point of junction of these 2 elements is subjected to greatest strain in case of a sudden severe blow to the chest cage displacing the thoracic structures by force of momentum. Others believed

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simply that the aorta is congenitally weaker in this area. Another factor to be considered is the transmission of the force of the blow by the confined, noncompressible blood.

CASE REPORT

J. R., a 21-year-old white man, was injured in an automobile accident March 6, 1949, while riding as a passenger in a car. He was found unconscious under the automobile, and was admitted to a near-by hospital where he was treated for shock. He remained unconscious for 24 hours but was discharged after 2 days' observation, a diagnosis of fractured ribs having been made. Five weeks later, while straining, he experienced sudden severe chest pain and was readmitted to the same hospital in a state of shock. Two blood transfusions were administered. He continued to complain of chest and back pain associated with weakness, loss of weight, and difficulty in swallowing. He was transferred to the Charleston General Hospital.

On examination the patient appeared emaciated, pale, and chronically ill. Dullness was present throughout the right lower chest. A systolic murmur was heard posteriorly over the right lower chest. Roentgenologic studies revealed a circumscribed mass in the posterior mediastinum and a well-defined mass in the right lower chest. The esophagus was displaced anteriorly, and the stomach displaced laterally.

A diagnosis of traumatic rupture of the diaphragm with right hemothorax was made. Exploration through a right thoracoabdominal incision after removing the eighth rib showed the pleural cavity to be filled with old, adherent blood clots. The diaphragm was intact. On removing the blood clots a massive arterial hemorrhage occurred. The tissues in this area were indurated and friable. Because of the critical condition of the patient, it was impossible to determine the source of the bleeding which, however, appeared to be coming from the posterior mediastinum. Several packs were inserted and the bleeding controlled.

One week later spontaneous bleeding occurred with the packs still in place. The patient was returned to surgery and exploration again carried out. The hemorrhage recurred and, in spite of repeated transfusions, the patient died just as the rent in the aorta was found.

Autopsy showed healed fractures of the sixth, seventh, and eighth ribs on the left side. A gaping tear was present in the aorta just proximal to the hiatal opening in the diaphragm. The defect measured 2.5 cm. in length and 1.4 cm. in width. The aortic wall, 0.2 cm. thick, was firm, elastic, whitish, and free of atheromatous plaques. There was no evidence of degeneration.

Histologic examination showed marked necrosis of the media surrounding the area of rupture. The remainder of the aorta was normal.

DISCUSSION

The case just reported was unusual in many respects. The time interval between injury and death was 81 days. Although multiple fractured ribs were present in the left thorax, all of the bleeding was confined to the right chest and mediastinum. Rupture of the aorta just proximal to the diaphragm, as was true in this case, seldom is seen.

The diagnosis of rupture of the aorta was not considered preoperatively. Successful closure of the defect in this particular case would have been extremely difficult if not impossible. Exposure of the proximal and distal segments of the aorta through the right chest could not conceivably be accomplished because of the fixation of structures in this area and the adherent blood clots. To have exposed the aorta through the left thorax would have necessitated collapse of the left lung. With the right lung already collapsed as a result of hemothorax, sufficient aeration would have been almost impossible.

SUMMARY

Of 90 cases of traumatic rupture of the aorta reviewed in the available literature, there were 64 deaths occurring within 1 hour following the injury. Only 7 patients survived for more than 18 hours. One case was reported in which the patient lived for 10 days.

A case of traumatic rupture of the aorta in which the patient survived for 81 days is presented. Death was caused by shock due to severe blood loss. Attempts at surgical repair of the rupture were unsuccessful.

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EXPERIENCES WITH THE ACUTE SURGICAL ABDOMEN IN THE PRESENCE OF THERAPEUTIC PNEUMOPERITONEUM

Report of Cases

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THE merits of pneumoperitoneum (either as definitive or complementary therapy) in the treatment of pulmonary tuberculosis have been well established. Increased intra-abdominal pressure alone or in conjunction with phrenic crush elevates the diaphragm and reduces pulmonary volume.[18] Although complications occur much less frequently than with pneumothorax[11, 19] they are of interest to the surgeon. These include: ascites,[11, 13, 19] aggravation of various types of hernia,[10, 13] atelectasis,[3, 9, 13] disappearance of intra-abdominal adhesions,[13] obliterative adhesive peritonitis,[2] puncture of bowel,[2, 10] tuberculous peritonitis, torsion of omentum,[19] hemorrhage into the spleen,[19] hemorrhage from the rectum,[7] peritoneal shock,[6] air embolus,[15, 16, 18, 20] puncture of omental veins,[4] a rather high incidence of appendicitis,[15] and pneumothorax.[2]

However, few reports have been made describing the acute surgical abdomen in the presence of artificial pneumoperitoneum. It is the purpose of this paper to present several such cases in patients recently treated in this hospital.

CASE REPORTS

Case 1.—H. B., a 44-year-old colored man, was treated during 1944 and 1945 in Cleveland City Hospital for far-advanced pulmonary tuberculosis with left phrenic crush and pneumoperitoneum. He was discharged in April of 1945 and treated with pneumoperitoneum refills every 10 days by a private physician.

On May 21, 1945, he was readmitted to Cleveland City Hospital because of severe epigastric pain. He had had a routine refill of air about 2 weeks previously. Three days before admission he was seized with severe pain in the epigastrium and following this he vomited 5 or 6 times. After the onset of the pain he noted severe abdominal distention and this apparently caused considerable dyspnea. During the 15 hours before admission he was unable to void or pass gas.

On admission the temperature was 36.6° C. and the pulse 140. Examination revealed the patient to be in shock. The abdomen was tremendously distended and tender throughout with some rebound tenderness. No peristalsis could be heard. The white blood cell count was 9,900 and the blood urea nitrogen was 46.2 mg. per 100 c.c. A diagnosis of perforated viscus with generalized peritonitis was made but the patient's poor condition precluded exploration.

Vigorous treatment of shock was instituted but the patient died 10 hours after admission. Post-mortem examination revealed acute suppurative peritonitis secondary to a ruptured gastric ulcer of the pylorus. The perforation was found to be patent and there was no evidence of walling off by omentum.

Case 2.—H. O., a 36-year-old white woman, was admitted to Cleveland City Hospital in 1941 with moderately advanced pulmonary tuberculosis and was treated with right

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phrenic nerve crush and pneumoperitoneum. She was discharged in September of 1942 and treated with pneumoperitoneum refills every 10 days.

On Oct. 15, 1945, 7 days after a routine refill with about 800 c.c. of air, the patient was admitted to Cleveland City Hospital because of pain in the lower right abdomen. Two days before admission the patient had noted severe paraumbilical pain and within 24 hours the pain had shifted to the right lower quadrant. No vomiting was described but there were several lose stools shortly before admission.

On admission the temperature was 37.8° C. and the pulse 90. Examination revealed localized tenderness on the right over McBurney's point with no associated spasm or tenderness. There was an obvious pneumoperitoneum. The white blood cell count was 6,350. A diagnosis of enterocolitis was made. However, acute appendicitis could not be ruled out and the patient was submitted to appendectomy under spinal anesthesia. The appendix grossly was found to be red, inflamed, and edematous; histologic sections revealed acute suppurative appendicitis.

The postoperative course was uneventful.

CASE 3.—J. M., a 45-year-old white man, was found to have minimal pulmonary tuberculosis in May of 1942, and was treated with bed rest. In October of 1944 a left phrenic crush was done and ambulatory pneumoperitoneum initiated.

On Dec. 15, 1945, 3 days after a routine refill, the patient was readmitted to Cleveland City Hospital complaining of dull pain in the epigastrium. The pain was of 18 hours' duration and followed the ingestion of dinner on the previous night. Despite a normal bowel movement he took a cathartic. On the morning of admission the pain shifted to the right lower quadrant and became constant instead of colicky and the patient had a shaking chill.

The admission examination revealed an acutely ill man. The temperature was 38° C., pulse 100, respirations 20, and blood pressure 130/80. The abdomen wasa distended and rigid. There was generalized tenderness throughout and there was tympany over the entire abdomen, most marked in the right lower quadrant. The urine was negative and the white blood cell count was 20,000.

The admission diagnosis was appendicitis but at laparotomy a perforated gastric ulcer on the lesser curvature near the pylorus was found. This was biopsied and closed, and the patient made an uneventful recovery.

CASE 4.—J. B., a 42-year-old white man, was operated upon in 1936 for adhesive obstruction of the small bowel and in 1938 for a perforated gastric ulcer. In 1942 the patient passed a kidney stone. In 1944 the patient was admitted to Cleveland City Hospital because of moderately advanced pulmonary tuberculosis with a positive sputum. Left pneumothorax was ineffective and accordingly a left phrenic crush was done and pneumoperitoneum was instituted. The patient was discharged Oct. 5, 1945, and pneumoperitoneum maintained on an outpatient basis.

On Feb. 23, 1946, 5 days after a routine refill, the patient was readmitted to Cleveland City Hospital because of abdominal pain of 8 hours' duration. The pain had developed suddenly, was localized to the epigastrium, and had gradually become more severe up to the time of admission. Definite radiation to the right shoulder was described. Shortly before admission the patient vomited once.

On admission the temperature was 37.3° C. and the pulse 104. Examination revealed the patient to be moderately dehydrated. There was spasm of the entire abdomen with rebound tenderness in the right lower quadrant. Liver dullness was absent. The white blood cell count was 24,000. A diagnosis of perforated ulcer was made and exploration carried out.

Under continuous spinal anesthesia, through a right rectus incision a perforated gastric ulcer on the prepyloric region of the anterior surface was noted and repaired. Numerous adhesions were encountered between the visceral and peritoneal wall.

The postoperative course was uneventful.

CASE 5.—G. H., a 27-year-old white woman, was found to have moderately advanced pulmonary tuberculosis in February of 1946. She was treated by phrenic crush and pneumoperitoneum and followed on an ambulatory basis.

On Aug. 8, 1946, she was admitted to Cleveland City Hospital because of severe epigastric pain. Her last refill was 2 weeks prior to admission. Twelve hours before admission she noted severe epigastric pain which shifted to the right lower quadrant. After the onset of pain the patient had a loose bowel movement and 6 hours later she vomited once.

The admission examination revealed a well-developed, well-nourished, acutely ill patient. The temperature was 39° C., respiration 32, and pulse 100. There was definite tenderness with minimal spasm in the right lower quadrant. The urine was negative and the white blood cell count was 26,100; 76 per cent were polymorphonuclears.

A preoperative diagnosis of acute appendicitis was made. Under spinal anesthesia an acute suppurative appendix was removed. The patient recovered uneventfully.

CASE 6.—J. F., a 19-year-old colored woman, was admitted to Cleveland City Hospital in March of 1944 with far-advanced pulmonary tuberculosis and was treated with right phrenic crush and pneumoperitoneum. During July of 1947 the patient was treated for acute salpingitis.

On July 28, 1947, 6 days after a routine refill, the patient was readmitted to Cleveland City Hospital with a 2 week history of right-sided pain, vomiting, chills, and menometrorrhagia. The last menstrual period began June 15, 1947, and bleeding had persisted to the time of admission. The pain was steady, severe, and localized to the umbilicus, gradually becoming more severe up to the time of admission.

On admission the temperature was 39.5° C. and the pulse 134. Examination revealed the patient to be acutely ill, with tenderness in the lower abdomen and a fullness in the cul-de-sac and in the right adnexal region. The cervix was tender on motion. The white blood cell count was 13,500 and the red blood cell count 2.16 million. A diagnosis of tuberculous salpingitis was made. However, the possibility of an ectopic gestation could not be ruled out and exploration was carried out.

On July 29, 1947, under spinal anesthesia a posterior colpotomy revealed dark red blood. Exploratory laparotomy through a low midline incision revealed a ruptured tubal pregnancy on the right. Salpingo-oophorectomy was carried out.

The postoperative course was uneventful except for fever during the first 11 days.

CASE 7.—E. F., a 23-year-old colored man, was found to have moderately advanced pulmonary tuberculosis during 1947 and was treated with pneumoperitoneum, phrenic crush, and bed rest at a sanatorium.

On Jan. 19, 1948, the patient was admitted to Cleveland City Hospital because of abdominal pain. Two days before admission and 24 hours after a routine pneumoperitoneum refill he had developed paraumbilical cramping pain. This was followed shortly by vomiting and a shift of pain to the right lower quadrant.

On admission the temperature was 38.5° C. and the pulse rate 110. Examination revealed an acutely ill patient witih a distended abdomen and tenderness and spasm over McBurney's point. Rectal examination revealed tenderness high on the right. The urine was normal and the white blood cell count was 14,600 with 72 per cent polymorphonuclears.

A diagnosis of acute appendicitis was made and the patient was operated upon under spinal anesthesia. An acutely inflamed appendix was removed.

The postoperative course was uneventful.

CASE 8.—L. N., a 29-year-old colored man, was found to have pulmonary tuberculosis in March of 1948 while hospitalized for an inguinal herniorrhaphy. In July of 1948 ambulatory pneumoperitoneum was initiated. On this treatment the right inguinal hernia recurred but remained easily reducible.

On Sept. 1, 1949, he was readmitted to Cleveland City Hospital because of a "painful rupture." The last pneumoperitoneum refill had been 1 week before admission. Five hours before admission the patient noted the onset of moderately severe pain in the right inguinal region while walking. Two hours later sharp paraumbilical pains were noted and the patient became aware of his inability to reduce the hernia.

Although the admission examination revealed a normal temperature, pulse, and respiration, the right inguinal mass was irreducible. The abdomen was not remarkable except for slight tenderness in the extreme right lower quadrant and absent bowel sounds.

The urine was normal and the white blood cell count was 10,500 with 81 per cent polymorphonuclears.

A diagnosis of recurrent right indirect hernia with possible strangulation was made and an emergency herniorrhaphy performed. After the incarceration was released the bowel was determined to be viable and was replaced, and the hernia repaired.

The postoperative course was uneventful.

CASE 9.—H. M., a 58-year-old white man, was found incidentally to have pulmonary tuberculosis during January, 1949, when he was operated for a scrotal mass which was also found to be tuberculous. He was treated with streptomycin, started on pneumoperitoneum, and maintained on bed rest at a sanatorium.

On Sept. 13, 1949, 1 week after a routine pneumoperitoneum refill, the patient was transferred to Cleveland City Hospital because of acute epigastric pain of 6 hours' duration. The pain was sudden in onset, intense, and localized to the epigastrium. Simultaneously with the onset of the pain in the epigastrium pain was felt in the left shoulder, but this pain was much more severe than the pain ordinarily felt with pneumoperitoneum refills. The patient said that 12 years before he had been treated for epigastric distress by being put on a diet of milk and crackers.

On admission the temperature was 38.2° C. and the pulse 110. Examination of the abdomen revealed generalized boardlike rigidity and abdominal tenderness. Distention was mild and no masses were palpable. The white blood cell count was 7,400 with 90 per cent polymorphonuclears. Radiographs of the abdomen revealed air under the diaphragm. Electrocardiographic tracings were suggestive of myocardial impairment, but no acute progress.

A diagnosis of perforated peptic ulcer was made and the patient was operated upon under spinal anesthesia 13 hours after the onset of symptoms. A small 3 mm. perforation was found in the anterior wall of the stomach in the pars media. Biopsy and closure of the perforation were carried out. The biopsy was reported as representing a chronic gastric ulcer.

Postoperatively the patient had an uneventful course until the sixteenth day, when he died suddenly. Post-mortem examination revealed the cause of death to have been a large pulmonary embolus. The ulcer site had healed completely.

DISCUSSION

The signs and symptoms of acute intra-abdominal disease might conceivably be altered somewhat by the presence of air under pressure in the peritoneal cavity. An elevated diaphragm, variable amounts of peritoneal fluid, and large subhepatic air spaces might effect fibrinous exudation and prevent the omentum from sealing off inflammatory processes. Since a significant number of patients are being treated with pneumoperitoneum we were interested in evaluating the acute surgical abdomen in these patients.

In most instances it was noted that the history and physical findings were typical in spite of the pneumoperitoneum. Appendicitis occurs in fairly typical fashion with a history of paraumbilical pain followed by nausea and vomiting and shift of pain to the right lower quadrant. In 3 of the 4 cases of perforated ulcers the onset was typically sudden, and in 2 of the cases the telltale shoulder pain was also described.

TABLE I.

CASE NUMBER	AGE	SEX	RACE	PREOPERATIVE DIAGNOSIS	TREATMENT	POSTOPERATIVE DIAGNOSIS	LAST REFILL	WHITE BLOOD CELL COUNT	RESULT
1	44	M	C	Perforated viscus	Symptomatic	Perforated gastric ulcer with generalized peritonitis*	2 weeks	9,900	Died 10 hours after admission*
2	36	F	W	Enterocolitis (appendicitis could not be ruled out)	Appendectomy	Acute suppurative appendicitis	7 days	6,350	Good
3	45	M	W	Acute appendicitis	Gastrorrhaphy	Perforated gastric ulcer	3 days	20,000	Good
4	42	M	W	Perforated ulcer	Gastrorrhaphy	Perforated gastric ulcer	5 days	24,000	Good
5	27	F	W	Acute appendicitis	Appendectomy	Acute suppurative perforation, peritonitis	2 weeks	26,100	Good
6	19	F	C	Tuberculous salpingitis	Salpingectomy	Ruptured tubal pregnancy	6 days	13,500	Good
7	23	M	C	Acute appendicitis	Appendectomy	Appendicitis, acute and chronic	3 days	14,600	Good
8	29	M	C	Strangulated inguinal hernia	Herniorrhaphy	Incarcerated inguinal hernia	1 week	10,500	Good
9	58	M	W	Perforated peptic ulcer	Gastrorrhaphy	Perforated gastric ulcer	1 week	7,400	Postoperative course uneventful until 16th postoperative day; died of pulmonary embolism*

*Autopsy.

Spasm, rigidity, and rebound tenderness, either alone or in combination, are conclusive signs of peritoneal irrigation. In this series one or the other of these signs was present in each case. The absence of any marked spasm in patients with acute appendicitis can be readily explained. Air prevents contact between the parietal peritoneum of the anterior wall and the inflamed appendix and spasm does not develop.

The degree to which pneumoperitoneum affects the protective function of the omentum cannot be evaluated from this series. In the patient (Case 1) who died of generalized peritonitis secondary to a perforated gastric ulcer, the ulcer was found at autopsy to be patent without any covering of omentum. In the remaining patients operative intervention was carried out too quickly to allow for observations on the function of the omentum, although omental covering seemed to be conspicuously absent from the inflammatory areas.

Some authors have noted a definite increase in the incidence of appendicitis in patients with therapeutic pneumoperitoneum,[15] while others have denied this.[11] Because in this city many patients are treated with pneumoperitoneum on an ambulatory status the exact incidence of appendicitis in this group could not be determined.

In Case 6 the differential diagnosis was a difficult problem. Although pregnancy occurs readily in patients with pneumoperitoneum,[12] ectopic gestation has not been reported.

In this series of cases all the patients except 1 were subjected to operation (Table I). Although the preoperative diagnosis was wrong in 3 of the 9 cases the signs and symptoms in all instances were of such a nature that in none could the diagnosis of acute surgical abdomen be excluded with enough certainty to avoid operation. In Case 2 enterocolitis seemed the most likely diagnosis but appendicitis could not be excluded and at exploration suppurative appendicitis was found. In Case 3 it was fairly obvious that the patient had generalized peritonitis and that surgery was in order although the exact etiology was not clear; a perforated ulcer rather than acute appendicitis was found at operation.

In 8 of the 9 cases the sputum at the time of the patient's admission was negative and did not contribute to the correct diagnosis.

SUMMARY

1. Nine cases are presented which feature the acute surgical abdomen when complicated by the presence of therapeutic pneumoperitoneum.

2. Therapeutic pneumoperitoneum does not greatly alter the clinical picture of the acute surgical abdomen.

3. Early surgical intervention is imperative in patients with therapeutic pneumoperitoneum who present symptoms and signs suggestive of the acute surgical abdomen. There is evidence to suggest that the function of the omentum and the response of the peritoneum are somewhat altered by the therapeutic pneumoperitoneum.

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Editorial

A New Role for Bacteria

In 1933, Tillett reported that he found in a culture medium sustaining a strain of pathogenic hemolytic streptococci a material which, in a highly specific manner, liquefied human blood clot. Fifteen years later, in 1948, he announced that the material had been purified sufficiently to be used in selected pathologic situations in patients. The most significant use from a surgical standpoint is in clotted hemothorax. A small amount of the material injected into a clot in the pleural cavity brings about liquefaction in a matter of hours. Thus, simple aspiration of the fluid permits expansion of the lung and restoration of respiratory function. In a number of patients in whom the lung is imprisoned by organized fibrin clot the operative decortication will be unnecessary.

Further, and more exciting, Tillett and his fellow workers discovered in the broth medium a new principle elaborated by the same streptococcus. This fraction liquefies thick purulent exudate. The latter principle has been shown to be an enzyme, desoxyribonuclease, which acts on the gelatinous material in pus, desoxyribonucleic acid. Living leucocytes which are actively phagocytizing are not injured by the enzyme. By this mechanism it has been demonstrated that purulent membranes interfering with lung expansion can be drawn off by aspiration.

The fibrin clot liquefaction is not a direct enzyme-substrate mechanism, but more likely an activation of some enzyme system already present in human blood.

The study of bacterial products in culture medium of this organism has scarcely begun. For example, varying quantities of hyaluronidase and other enzymes are present; unexplained reactions on fresh wound surfaces and other phenomena indicate the presence of still other enzymes, all of which are being studied.

Tillett rightly has termed the action of these bacterial products on inert clot and exudate "enzymatic débridement." The commercial distribution of large quantities of streptokinase and streptodornase made by vats full of streptococci will begin shortly. Thus, the pathogenic organism has been converted into a factory for the production of most exquisitely precise chemical surgical tools which can destroy the fibrin clot or the dead purulent exudate.

The surgeon's imagination is taxed to encompass the possibilities for the extension of this new field.

Can the fibrinolytic principle be extended to intravenous use in human beings? Can such material be brought into contact with a clot within the walls of the coronary arteries? or cerebral arteries? Are other organisms producing

enzymes which may digest dead connective tissue or dead bone or dead skin? Will it be possible to bring about accurate and rapid débridement of dead tissue in burned areas with a battery of enzymes, each one acting in its own substrate?

It is pertinent to point out that the information advanced and the possibilities presented by this work resulted from inquiry into the biology of a lowly objectionable bacterium. The end point of long untrammeled research is not predictable.

In a war against pathogenic organisms, to turn the enemy guns to our own good purpose is first-rate strategy.

—*John H. Mulholland, M.D.*

Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

THE HEALING OF SOFT TISSUE WOUNDS; THE EFFECTS OF NUTRITION, ANEMIA, AND AGE

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INTRODUCTION

DURING the course of his existence, man, in common with other living creatures, is subject to frequent injuries. It is to be expected, therefore, that the human organism, to be successful as a going concern, should possess mechanisms to repair the physiologic and pathologic damage sustained. Not the least important of these mechanisms is the ability to restore continuity to damaged tissues. The subject of wound healing has long interested physicians and surgeons, but only recently have there been attempts to elucidate the many variables governing this process. It is the purpose of this paper to review critically the work reported on the effects of three of these variables, namely, nutritional status, anemia, and age on the healing of soft tissue wounds. This review was undertaken as a preliminary to experimental studies contemplated in this laboratory.

DEFINITIONS

By wound repair is meant the sum total of the processes involved in the restoration and maintenance of continuity in disrupted tissues. While the implications of the terms which have been used to describe the separate processes are fairly clear-cut, their exact meanings are somewhat clouded in the literature because of ill-defined and inconsistent usage. It is well, therefore, at the start of this discussion, to define these terms.

The term cicatrization will be used to denote the total process of wound healing, having as its component parts epithelization and contraction. The relative importance of these varies for different types of wounds and for different species of animals. The term contraction has been the special object of confusion because of the failure to differentiate between two main types of contraction, namely, early and late. Early contraction includes shrinkage of the fibrin deposited in the wound and of the elastic elements in the surrounding tissues. Early stages of wound closure include not only these phenomena of initial contraction but also those of early migration and enlargement of the bordering epithelium to be described below. The early phase of contraction

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is of particular importance in the healing of surface wounds but may also play a lesser role in the healing of incisions. Late contraction results from the organization of the fibrin exudate through the migration, proliferation, and maturation of capillaries and of fibroblasts, and the formation and maturation of intercellular matrix.

Epithelization refers to the formation of an intact epithelial membrane over the wound surface. According to Loeb[67, 84] and Hartwell[35] this process is initiated by the elongation and ameboid migration of cells from the prickle layer of the healthy skin surrounding the wound. The basal cells apparently do not take part in this migration. Hartwell designated the prickle cell as the "primary epithelial cell." According to him, mitotic division plays a secondary role in the formation of the healing membrane in that mitoses are not observed in any great number until the wound has closed or until the fifth day of healing. They are then seen chiefly in the cells of the surrounding skin and only to a lesser degree in the membrane itself. The new basal layer appears late and is apparently formed from the prickle cells which have already migrated. Somewhat stronger emphasis is placed on the role of mitoses in epithelization by earlier writers such as Spain and Loeb[84] and Akaiwa.[2] They maintained that mitosis is initiated early (during the first two days) in response to the pull of migrating epithelial cells presumably in the malpighian layer, and that proliferation is finally brought to a halt by increasing pressure of the epithelial plates as they approach one another over the wound surface. It would appear that multiplication of epithelial cells becomes of increasing importance as the size of the surface defect is increased.

While adequate descriptions of the morphologic changes in wound healing may be found in standard texts, it is felt that certain aspects warrant further discussion. Initially, it should be stated that in the past there has been a tendency to consider automatically the results observed in the healing of wounds in one species of animals as applicable to the healing of wounds in another species. In addition, the processes in the healing of different types of wounds, such as superficial ulcers and deep incisional wounds, have been equated without question. Although these processes may have certain features in common, one has no assurance that laws, descriptions, and formulas found applicable in the one instance are necessarily applicable in the other.

Carrel[17, 18, 20] divided the process of wound healing into four parts: (1) the quiescent period; (2) period of granulous contraction; (3) period of epidermization; and (4) "cicatrical" period. This description resulted from extensive studies of the healing of surface wounds in animals and man. Carrel measured the change in granulating surface areas at four-day intervals, attempting to measure separately contraction and epithelization. The junction of the epithelium and granulating surface and the outer edge of the wound were both traced on cellophane and the areas measured with a planimeter. Similar data were collected by Clark[21] in dogs. Upon examination of the data of Carrel, Du Nouy[26, 27, 28] concluded that the cicatrization of sterile wounds could be studied in the same way as ordinary physiochemical phenomena. This

reasoning was based not only on a consideration of the geometric form of the curves of wound healing, but also on the fact that a rise in temperature of 10° C. increases the rate of cicatrization about twice, which would be expected if the process of wound healing depended on chemical reactions.[29] Du Nouy found it possible to express the course of cicatrization by a mathematical equation and he formulated an index of cicatrization (''i''), a constant characterizing each wound. This constant is larger the smaller the wound and the younger the subject. With his formulas Du Nouy was able to predict a theoretical healing curve for surface wounds. It was felt by Du Nouy and Carrel that since this curve was an expression of what should happen to an uninfected wound in a normal man, it might be used as a basis of comparison with what actually does happen in any given case, thereby enabling one to study accurately the fluctuations of cicatrization in a given individual. Although it is clear that the size of the wound and the age of the patient are important factors in the healing of aseptic open wounds, there is no evidence that the Du Nouy formulas are applicable at the present time to human wound healing, despite the fact that some recent publications have assumed them to be so without corroboration.[42, 91] Other mathematical formulas have been described by other authors, but their general validity and applicability are as yet not clear.

While the observations of Carrel and Du Nouy on the healing of wounds seem valid in general, certain of their conclusions are open to criticism. Carrel stated, for instance, that wounds of equal size in patients of different ages heal at the same rate. However, he also made the observation that the healing curves of wounds of unequal size tend to approach each other, so that the time required for complete healing is about equal for the two. In one case cited, two wounds of unequal size healed at such a rate that repair of the larger actually preceded that of the smaller by two days. It would appear that these two concepts are inconsistent. It should also be pointed out that the quiescent period described by Carrel varies markedly among different species; for example, Waterman and associates[91] found that the lag period in the healing of open wounds in rats is less than twenty-four hours, whereas the usual lag period in dogs has been described as three to four days.

Another mathematical analysis of the healing process, this time of the incisional wound, has been provided by the work of Harvey and Howes.[39, 48] Many natural phenomena (such as growth of a population or individual growth of bacteria in a culture) are mathematically described by the well-known sigma curve, the initial flat portion representing a ''lag'' phase, the steep portion of the curve representing a logarithmic or accelerated phase, and the terminal flattening portraying the growth retarded phase. It was of interest to know whether the process of healing could be represented by a sigmalike curve or whether it more nearly approached the pattern of a simple monomolecular reaction—namely, one of continuous deceleration from peak velocity attained initially after the latent phase. The latter pattern is in fact similar to the curves described by Carrel and Du Nouy from simple observation of surface wound closure.

With tensile strength measurements of fibroblastic proliferation in incisional wounds as the criterion for wound healing, Harvey and Howes found in adult animals that the rate of gain in tensile strength decreased steadily from an initial peak velocity. They pointed out that after a four-day latent period, the tensile strength of a wound begins to rise and reaches one-third of its final value by the sixth postoperative day, two-thirds around the eighth day, and attains maximum strength by the twelfth to fourteenth day. It cannot with certainty be stated whether this observation indicates that the healing of incisional wounds follows the pattern of a simple monomolecular reaction or whether it represents the growth retarded phase of a sigma-type curve, the accelerated phase of which may have been undetected. That the latter alternative may obtain is suggested by further observations of Harvey and Howes[47] that the healing curve of incisional wounds in young rats showed a short (two- to three-day) accelerated growth phase. If observations could have been appropriately timed, it is possible that a brief accelerated phase might have also been detected in adult animals. Similar reasoning might be applied to the observations of Carrel on the healing of surface wounds, since he was wont to make observations only at four-day intervals. Kobak and associates[53] recently restudied abdominal incisional wounds in rats and actually found an accelerated phase in adult animals, including both normal controls and experimental protein-deficient animals. The reason for this discrepancy between Kobak's data and those of Harvey and Howes is not clear at the moment, although it may be found in the difference in wounds studied and in techniques of measurement, for Harvey and Howes used simple distention of the incised stomach with air, while Kobak used distention of the incised abdominal cavity with an air-filled condom. With the data at hand definite conclusions cannot now be reached as to the type of curve followed by the normal healing wound.

Various methods have been evolved for the measurement of wound repair. Simple observation has been widely used for both surface and incisional wounds. It is especially valuable in the case of the former, where serial observations (either tracings or photographs) may be employed to determine the changing size of wound area. Recently, methods have been introduced to study surface wound healing uncomplicated by contraction. Howes[45] measured the rate of progression of an epithelial island left in the center of a skin defect, while Marshak[71] employed a transparent plastic (methacrylate polymer) painted over the wound and the surrounding intact epithelium. This substance dries without shrinkage and acts as a splint for the defect, preventing contraction and allowing the course of epithelization to be followed. It should be pointed out that this is definitely an unphysiologic situation.

Histologic examination has been extensively used for the investigation of wound healing. Serial biopsies may be used as a rough quantitative guide for the estimation of epithelial and fibroblastic progression. Special stains have been used to study connective tissue maturation; for example, while immature collagen is argyrophilic, mature fibers fail to take up silver but react to dyes such as van Gieson's stain to which immature fibers are inert.[50]

Progression of healing in incisional wounds may also be followed by serial measurements of tensile strength. This may be accomplished either by recording the force necessary to separate the edges of an excised wound by application of weights,[7, 8, 13, 99] or, if the wound has been made in the wall of a cavity (such as the abdomen or stomach), the air pressure required to disrupt the wound may be measured by a manometer as the hollow space is inflated.[36, 40, 49, 59, 87] The technique of Kobak and co-workers[53] of distending the abdominal cavity by means of an air-filled condom is an improvement over the older technique of distention of the abdominal cavity by the direct introduction of air. This is particularly true in the later stages of wound healing when the wound has become stronger than the pelvic peritoneum. It should be pointed out that these techniques are, at best, approximate, and all data so obtained must be subjected to careful statistical analysis, which has not been done in most reported studies.

Lately, radioactive tracer elements, especially phosphorus, sulfur, and strontium, have been employed experimentally to assay cellular formation in wounds of liver, skin, and bony tissues.[72] Upon parenteral injection of these elements, their accumulation at the site of injury may be followed with a Geiger counter and these counts compared with those in control areas of normal tissue. This technique has not been used widely nor adequately evaluated as yet.

Having considered some of the general principles underlying soft tissue wound repair and its measurement, it is now our intent to consider the influences of the nutritional status, anemia, and age of the wounded individual on the healing process.

NUTRITIONAL STATUS

Protein

In any consideration of nutrition and repair, protein metabolism is a logical point of departure, since repair implies cellular proliferation which in turn requires protein as the principal building constituent. It has been known for centuries that certain poorly nourished patients are subject to delay in, or failure of, healing of wounds. However, except for some observations in relation to scurvy there were few accurate studies until recently.

In 1919, Clark,[21] at Johns Hopkins Hospital, reported experiments on twelve mongrel dogs, three of these on each of four diets: (1) high protein diet—500 Gm. of lean meat, beef, or liver; (2) high carbohydrate diet—500 Gm. of bread; (3) high fat diet—300 Gm. of fat and 100 Gm. of bread; (4) mixed diet (fat, lean meat, bread).

The dogs were fed on these diets for three days prior to operation and during the postoperative method. Weights remained stationary and the dogs appeared normal throughout the experiment. At operation under ether anesthesia, two small surface wounds of unequal dimensions (exact sizes not stated) were made on the shaved backs by excision of circular skin flaps. No dressings were applied to the wounds. Measurements of the wound area were made by cellophane tracings at three- to four-day intervals.

A second set of similar wounds was made as soon as the first had healed and immediately upon healing of the second set of wounds, a third set was made. The diets were interchanged simultaneously with the making of the third set of wounds.

Clark found the curve of wound healing to be similar to that described by Carrel. There was a lag period which varied in time, depending on the diet used (Fig. 1). The animals on the high protein diet were reported as showing no lag period, those on the carbohydrate diet a lag period of three days, those on fat, six days, and those on the mixed diet a lag period of four days. The most marked differences, then, were between the group on the high protein diet and that on the high fat diet.

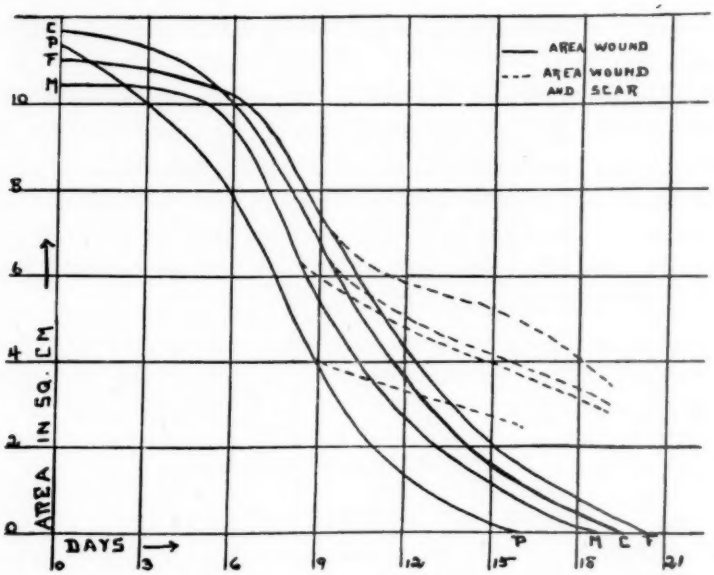

Fig. 1.—Curves of healing of surface wounds on dogs eating different diets: *C*, high carbohydrate; *P*, high protein; *F*, high fat; and *M*, mixed. Area of wound and scar --------; area of wound ————; abscissa, time in days; ordinate, wound area in sq. cm. "The progress of Period III, the period of epidermization, is shown, the dotted line indicating the area of the wound and the scar, the heavy line the wound area. It is evident that the formation of the epithelium starts on the same day, irrespective of the diet and the size of the wound." (From Clark, [21] Bull. Johns Hopkins Hosp.)

Amazingly enough, when the diets of the protein and fat groups were interchanged, no quiescent period was noted in those shifted from fat to protein, while a six-day lag period was seen in the other group. The length of the quiescent period was found to be the only variable inasmuch as healing curve increments ran roughly parallel after the actual onset of wound closure. A visible epithelial membrane was first noted on the ninth day in all cases.

Certain factors must be considered in the interpretation of Clark's data. First, the time required for healing varied from about fifteen to twenty days for each set of wounds, so it is evident that some of the dogs were maintained on what unquestionably were partially deficient diets for periods of one or two months. Second, Clark allowed only a three-day period on the special diets before the first set of wounds and, as mentioned, the third set was made simul-

taneously with the change of diet. That any metabolic effects should appear after such short preliminary test periods seems remarkable. In addition, it will be recalled that the wounds were measured at three- to four-day intervals. Consequently, it is possible that there might have been a lag period of at least two days in the high protein animals. Third, only the average progress of healing for each group is plotted in Clark's paper, with no reference as to "spread"; consequently, statistical evaluation is not possible. Finally, Clark's work has been generally interpreted by subsequent workers to indicate that a high protein diet stimulates wound healing, while a high fat diet inhibits it. However, in the latter case, the important factor may be not that fat intake is high but that the protein intake is very low.

After Clark's work there followed a gap of ten years until Harvey, Howes, and their co-workers began their studies on wound healing. In contrast to Carrel's and Clark's studies which had been made on open wounds, Harvey and Howes studied the healing of sutured surgical incisions. In their early studies[40, 49] they observed that the tensile strength of the healing incision was a function of the multiplication and maturation of the fibroblast and intercellular substance, and that the development of tensile strength ran parallel in different tissues, that is, skin, fascia, and stomach. Thereafter they concentrated on measurements of tensile strength of stomach wounds as an index of the course of healing. Their general technique was as follows:

Under ether anesthesia a wound about 1 cm. in length was made through the anterior surface of the stomach of rats, transversely to the long axis at the junction of the middle and lower one-third. The edges were approximated in two layers with number 000 plain catgut which was known to disappear in three days.

At varying intervals animals were killed with ether. The esophagus was tied, the stomach removed and kept moist with saline solution. A cannula was inserted through the pylorus and connected to a pressure line with a mercury manometer recording on a revolving drum. The pressure at the breaking point of the wound or stomach was thus automatically recorded by a sharp drop in pressure. This technique gives no absolute value of wound strength but only relative differences.

Harvey and Howes found that under ordinary circumstances there is a latent period of approximately four days before healing becomes appreciable in terms of these functions. It is during this period that the strength of the wound is dependent solely on the holding power of the sutures employed. The end of the latent period is marked by the abrupt beginning of the period of fibroplasia, which immediately acquires its maximum velocity. Thereafter, in adults, the velocity of growth is constantly and progressively diminishing until the maximum strength is attained. This usually requires two weeks in normal animals. The point of maximum strength is defined as the point at which the rupture of the stomach takes place elsewhere than at the wound.

Harvey and Howes[40] compared the healing of wounds in adult rats on a standard Sherman diet with that in adult rats on a high protein diet. The

composition of the standard diet in terms of calories was as follows: protein 13.8 per cent, carbohydrate 39.2 per cent, fat 47.0 per cent. The high protein diet was: protein 68.7 per cent, fat 31.8 per cent (80 per cent casein, 12 per cent Crisco by weight).

The animals were kept on the diet one week preoperatively, fasted for six hours preoperatively, but postoperatively the food was resumed as soon as possible. The caloric intake was slightly less in the animals on the high protein diet.

Harvey and Howes observed no effect of the high protein diet on the lag period but rather an increase in the rate of development of tensile strength during the period of five to nine days postoperatively. This contrasts markedly with the results of Clark. It is possible that the higher percentage of fat in Harvey and Howes' cases may account in part for this difference, since Clark's dogs on the high protein diet received very little fat, whereas Harvey and Howes' rats received as much as 30 per cent of the calories from fat. In addition, of course, the types of wounds studied were different, as well as the species of animals used.

Harvey and Howes also observed that the high protein diet shortened the time required to reach the end point of the curve from the thirteenth to the eleventh day, the end point being arbitrarily chosen as the point where all the breaks occurred elsewhere than at the wound. The ultimate maximum breaking strength was, however, approximately equal in the two groups.

There are no studies of the effects of high protein diets on the healing of wounds in young, growing animals.

Acute Protein Deficiency.—Howes and associates[46] observed the effect of complete and partial starvation on the rate of wound healing in both young and adult rats. The partially starved animals were placed on the diet one week before operation, but those completely starved were not placed on their water diet until the day before operation.

Stomach wounds were inflicted as described previously. It was found that the healing curves of adult rats on control diets and of those under conditions of partial or complete starvation were roughly parallel. A slight terminal rise in daily tensile strength increments was, however, noted in the completely starved group. Further, this was obviously a relatively acute experiment during which, as was later suggested by Howes,[44] it is doubtful whether true hypoproteinemia could have developed. Harvey and Howes suggested that the terminal rise noted in the daily tensile strength increment in the completely starved adult may have been the result of an agonal increased catabolism of body protein incident to complete starvation, making increased quantities of protein products available to areas requiring protein for tissue synthesis.

Another explanation, suggested by the observations of Herrmannsdorfer[41] and of Reimers and Winkler,[78] is that acidosis tends to increase the rate of wound healing. Presumably starvation predisposes to the acidotic state, although, as has been pointed out by Harvey and Howes, true acidosis has yet to be observed in the rat.

A final possibility was suggested by Howes from the work of Morgulis[75] who believed that a reduction in cell cytoplasm without a proportional reduction in nuclear size (the condition presumed to exist in starvation) tended to result in an increased rate of cell division in an effort to restore normal relations.

When wounds were studied in young, actively growing rats on an inadequate diet, totally different results were obtained. The young rats did not withstand complete starvation long enough for their wounds to give satisfactory determinations of healing strength. In the partially starved group there was a marked retardation of wound healing and the final portion of the curve was not reached till the thirteenth day.

Chronic Protein Deficiency.—Thompson, Ravdin, and Frank[88] showed that in dogs made protein deficient (as indicated by plasma protein concentrations of 3.5 Gm. per 100 ml. and by delayed gastric emptying times) by the use of low protein diets and repeated plasmapheresis, abdominal incisions healed poorly, disrupted frequently (72 per cent), and demonstrated on macroscopic and microscopic examination marked intercellular edema and delay in fibroblastic proliferation even as late as the fourteenth postoperative day.

It was evident to these investigators that these dogs suffered in two important regards: (1) they had been for some time in negative nitrogen balance and had, in general, nutritional deficits of protein, and (2) their colloid osmotic pressures were seriously reduced with a resulting disturbance in the relation between intravascular and extravascular fluid. To clarify the situation further, additional studies[89] were made. Three dogs made similarly hypoproteinemic preoperatively were given repeated infusions of lyophilized plasma postoperatively, 300 c.c. daily for six days and 100 c.c. daily for the next four days. The plasma protein concentration rose to normal by the seventh day. Biopsies and gross observations on the seventh and fourteenth days revealed apparently normal wound healing.

In the next study[79] seven dogs were prepared in whom the plasma protein levels were below 3.5 Gm. per 100 c.c., but to whom enough acacia was given to prevent edema. The concentration of acacia was maintained between 2 and 3.6 Gm. per 100 c.c. Biopsy specimens were taken on the seventh and fourteenth days. All the wounds showed definite fibroplasia, and apparently healed in normal fashion. No experiments were done in which acacia was given to normal animals.

It was evident from these experiments that the formation of fibroblasts is not solely a function of the concentration of the serum proteins. In fact, in the last three animals which received acacia the protein concentration dropped respectively from 3.67 to 1.91, from 3.55 to 1.99, and from 3.11 to 2.08 Gm. per 100 c.c. within seven days after the administration of the first infusion of acacia solution, and yet healing progressed in an apparently normal manner.

The following hypotheses were suggested in explanation of the effect of the acacia: (1) The relation of hypoproteinemia to wound healing is mainly on an osmotic basis. The acacia corrects the low colloid osmotic pressure of

the serum, with the result that fibroplasia occurs. However, in earlier experiments it had been found that some definite fibroblastic repair was noted in spite of intercellular edema, and at that time it was felt that edema per se did not explain the delayed wound healing in the hypoproteinemic dogs. It should be pointed out, however, that doubtless the quantity of edema is important in this regard. (2) The relation of hypoproteinemia to wound healing is mainly on a nutritional basis, but the administration of acacia makes it possible for more protein to be withdrawn from the plasma for tissue building purposes. The liver in these experiments appeared to be full of acacia on histologic examination. The acacia may reduce the affinity of the liver for labile protein and thus make available for tissue repair a larger proportion of the products of normal protein catabolism. It should be stressed that there is no evidence to support these theories.

In consideration of the results of Thompson and co-workers it should be borne in mind that the criterion of wound healing used was solely gross and histologic appearance, and that the latter was limited to the seventh and fourteenth postoperative days. No measurements of tensile strength were made. In addition, there were very small numbers of animals in the different series. Finally, the size of the wound made is very important, since small incisions made in similarly hypoproteinemic dogs prepared for fracture studies healed in apparently normal fashion.[80]

Recently, the relationship of protein to wound healing was restudied by Kobak and his co-workers.[53] Chronic protein depletion in albino rats was affected by a diet low in protein (1.9 per cent) for a period of three months. The presence of hypoproteinemia was established by repeated plasma determinations and measurements of body weight. Plasma protein concentration varied between 3.2 and 5 Gm. per 100 c.c. and the weight loss between 20 and 40 per cent. Upper abdominal incisions about 2.5 cm. in length were made and closed with through and through steel wire sutures, and frequent tensile strength measurements were made during the first nine days postoperatively. Wound strength was measured by forcing air into an intra-abdominally placed condom. The initial point of wound separation was noted, as was the final pressure needed to force the condom through the disrupted incision. The difference between these readings was taken as the final "objective" measure of wound tensile strength, but it is difficult to know just what this arithmetical difference actually measures. This is to be contrasted with the work of Harvey and Howes, who used solely the initial separation of the wounds as the end point. Kobak's group demonstrated a difference in latent periods between the controls and the low protein animals, the controls having a lag period of three days, the low protein animals five days (Fig. 2). The curves otherwise were parallel. Among the deficient group there was no correlation between weight loss, plasma protein concentration, and tensile strength. A protein-depleted rat which had lost 20 per cent of its body weight exhibited as poor healing as its fellow which had lost 40 per cent of its weight. Likewise, rats with serum proteins as low as 3.2 Gm. per cent produced wounds with as great strength as those in similar

animals with serum proteins of 5.0 Gm. per cent. Following the lag period the tensile strength curves rose in parallel fashion reaching equal heights on the seventh and ninth days, respectively. Inspection of these curves, as previously stated, revealed that the period following the latent phase follows a growth accelerated type of curve, rather than the growth retarded form as found previously by Harvey and Howes in normal adult rats. The reasons for the dissimilar findings and their significance are not clear although the difference is possibly due to the facts that different types of wounds and different methods of tensile strength measurements were used.

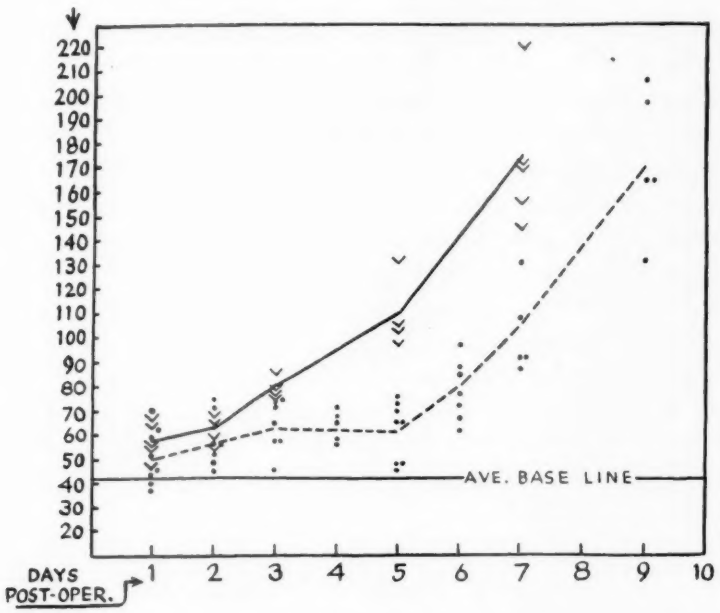

Fig. 2.—Comparison of tensile strength of wounds of the abdominal wall in protein-depleted and normal control rats. Control diet ————; low protein diet ---------. (From Kobak, Benditt, Wissler, & Steffee,[53] Surg., Gynec. & Obst.)

The lowered tensile strength of wounds in protein-deficient rats during the third and fifth postoperative days is apparently due to (a) diminution in the number of fibroblasts, a decrease in their rate of maturation, and a general failure of the fibroblasts to organize with adequate density along the lines of stress; and (b) delay in maturation of the reticulum into mature collagen. Tissue edema was absent in these animals and wound infection was not common; however, in the protein-deficient rats there was evidence of poorer resistance to infection, with occasional instances of abscess formation along the suture channels and occasional diffuse leucocytic infiltration.

An additional study was conducted by Kobak and associates in order to determine the influence of osmotic factors on the healing process. It was thought that the hypoproteinemic rats were in a compensated osmotic equilibrium because they showed no gross edema; however, minor osmotic fluctuations may have been present, and these possibly could have accounted for differences in tensile strength. Rats used for the determination of postoperative caloric in-

take were maintained on their respective diets for a period of three weeks after their initial operation, when they were reoperated upon on the opposite side. A filtered autoclaved solution of 6 per cent gum acacia was administered daily via the tail vein in doses of approximately 1 Gm. per kilogram of body weight. This probably resulted in a concentration of acacia similar to that obtained by Rhoads and associates[80] in their experiments in dogs previously mentioned. The results obtained were similar to those in the hypoproteinemic animals not receiving acacia. These results then are in marked contrast to those of Rhoads and co-workers who, it will be remembered, reported apparently normal healing in hypoproteinemic dogs given acacia. However, it may be that the results of the two groups of investigators are not actually incompatible since the criteria used by Rhoads and co-workers to estimate wound healing were only gross appearance and study of histologic sections taken on the seventh and fourteenth days. From Kobak's data it is apparent that fibroplasia in hypoproteinemic rats would be evident by the seventh day and that wound healing by the fourteenth day would be fairly normal if judged by similar criteria. While the exact role of edema as it affects wound healing is difficult to assay at the present time, certain tentative conclusions may be indicated. If one discounts species differences and variations of suturing techniques, it would appear that the important difference between Thompson's hypoproteinemic dogs which showed a high incidence of wound disruption and the hypoproteinemic rats of Kobak which did not was simply the presence in the dogs of manifest tissue edema. This, of course, was not evident in the rats. There are no studies to date reported on wound healing in animals in good nutritional status in whom edema has been artificially produced.

Localio and associates[66] have recently reported studies of the effect of *dl*-methionine on the healing of wounds in protein-depleted animals. Observations were made in young white adult rats, one group serving as normal controls, one group being depleted and rendered hypoproteinemic by means of diet, and a third group, after five weeks of similar depletion, given *dl*-methionine as the sole supplement to the protein-deficient diet. Each animal in this last group received 150 mg. methionine subcutaneously for ten days, the last injection of methionine being given twenty-four hours before the animal was sacrificed.

Aseptic wounds 3 cm. in length were made to the right of the midline in the upper abdomens of the animals. The wounds were closed with interrupted sutures of No. 36 steel wire. Animals were sacrificed daily from one to ten days.

A prolonged lag period, slowed proliferative period, and a delay of final healing were found in the protein-depleted, unsupplemented group. In the protein-depleted, methionine-supplemented group, there was a shift of the curve of wound healing toward normal, and, in fact, an apparent shortening of the lag period from three days in the normals to one day in the methionine animals. As an explanation for the effect of methionine Localio and associates suggested that the sulfhydryl radical is deficient and not readily available to the wound of the protein-deficient rat, and deficient SH enzyme activity may be one of the reasons for delayed healing. It is postulated that methionine would furnish the necessary SH groups.

In considering these results it should be pointed out that there are certain errors inherent in the method by which the tensile strengths of the wounds were determined. The peritoneal cavity was distended with air, and the "bursting pressure" of the wound measured. As Localio and associates pointed out, by this technique the mean maximum pressure that can be applied to the abdominal cavity of normal unoperated control animals is about 98 mm. of mercury, disruption of the pelvic peritoneum occurring at this point. In some of the hypoproteinemic and methionine-supplemented animals, the pelvic peritoneum ruptured at pressures appreciably less. It is clear then, that the maximum strengths of the wounds were not determined in all instances, and, in fact, in no instance in the control group after the fifth day. It should also be mentioned that there was a considerable variation in apparent tensile strength of the three groups in the first two days, a period during which, in past studies, tensile strength has been relatively constant and low in all experimental animals, being ascribed only to the holding power of the deposited fibrin. No histologic studies were made. Finally, normal animals given methionine supplements were not studied. However, the results reported were subjected to statistical analysis by the authors and appear statistically valid.

It is generally felt that patients in a poor nutritional state are apt to have impaired wound healing. However, there are relatively few good clinical studies bearing on this. Most reports have been analyses of cases of wound rupture, where attention is called to the fact that the highest incidence of wound rupture occurs in elderly cachectic patients with disease of the gastrointestinal tract, and it is inferred that the malnutrition present in these cases has predisposed to the impaired wound healing.[10, 22, 32, 37, 43, 51, 55, 73, 86, 93, 94] There are, of course, numerous other factors important in the pathogenesis of wound rupture, such as inadequate hemostasis, excessive tension, and so forth, which we shall not consider in this discussion.

As recently as 1940 Koster and Shapiro[56] found no reported studies on the relationship of the concentration of serum proteins to wound healing. In the next few years a few such reports appeared.[38, 54, 55] Koster and Kasman[54] observed a series of eighty patients, forty of whom had wound rupture. In general, the patients with deep infection or disruption of their wounds tended to have low total plasma protein concentrations and, particularly, low plasma albumins. However, Koster and Shapiro pointed out that the occurrence of normal concentrations of serum protein and albumin in some patients with disrupted wounds and of relatively low concentrations in many patients with clean and well-healed wounds indicates that hypoproteinemia by itself is neither a necessary nor sufficient condition for the development of wound rupture. In this regard it should be pointed out that the complex relationship of serum protein concentration to the nutritional state of the individual and the possible significance of serum protein levels must be considered. Interpretation of serum protein concentration values is often difficult. In surgical patients, particularly, one is frequently confronted by situations in which an acute disturbance has occurred in a patient with chronic protein deficiency. When this

happens, the acute changes may intensify or mask the chronic ones, depending on the direction of change. A patient who has depleted body proteins and, normally, a low plasma protein level may, by reason of vomiting, become dehydrated. Plasma protein concentration may then become normal. However, as the blood volume of such a patient is increased by the administration of electrolytes or by other means, the plasma protein concentration will be found to fall to low values.

The relative changes of albumin and globulin are also of importance. In general, in acute depletions from any cause the albumin is lost more rapidly and to a greater amount than the globulin and is built up again more slowly. A normal plasma protein value will mask a quite severe hypoalbuminemia when the globulin level is high. It must be remembered that except in acute loss the plasma proteins fall only after long-continued depletion. Therefore, in cases of chronic illness the presence of hypoproteinemia indicates a large tissue protein deficit. Elman found that a loss of 1 Gm. of albumin from the plasma represents a tissue loss of 30 Gm. of protein. Still higher ratios of plasma to tissue protein have been found.

Localio[65] recently reported a series of observations on the plasma and tissue protein concentrations (peritoneum, muscle, and fascia) of three groups of patients. The first series comprised a group of healthy individuals undergoing laparotomies for relatively uncomplicated conditions; the second series included patients who were suspected of being debilitated because of the nature of their illness—in general, serious gastrointestinal diseases; while the third series was made up of a group of patients whose wounds had ruptured. Localio and his co-workers observed that although the serum protein concentrations in the three groups were not markedly different, the tissue protein concentrations, particularly of the fascia, in the third group were significantly lower than the corresponding concentrations in the "control group." These analyses were done on wet tissues subject to variations in hydration and, therefore, in protein concentration, and it should be pointed out that their interpretation is beset with difficulties similar to those present in the interpretation of serum protein concentration.

Hypoproteinemia has been found in many of the patients with chronic ulcerations of the skin associated with phlebitis or varicose veins.[76] The administration of an adequate diet has resulted in a return of the plasma protein concentration to normal and a concomitant healing of the ulcers. Similar findings have been reported in patients with decubitus ulcers.[85]

The healing of peptic ulcers is, of course, different from the healing of ordinary incisional wounds and skin ulcerations. It is, however, of interest that several investigators have observed ulceration of the stomach in protein-deficient animals. Although peptic ulcers have not been observed in significantly increased numbers of malnourished individuals, patients with peptic ulcers at times have protein deficiencies often to the point of hypoproteinemia. Excellent symptomatic results and healing of ulcers confirmed by x-ray studies have been

reported in patients with previously intractable peptic ulcers who were given very high protein diets in the form of partially hydrolyzed protein.[23] It has been suggested that neutralization of the acidity of the gastric juice by the strong buffer action of the protein hydrolysates, relief of digestive effort on the part of the gastrointestinal tract, and the provision of essential protein constituents for tissue repair are the factors responsible for the prompt response to this hyperalimentation regime. Others are not impressed with the efficacy of oral protein hydrolysates.

Fig. 3.

Fig. 4.

Fig. 3.—Absent granulations in an extensively burned, poorly nourished child. (Courtesy of Levenson and Lund.[63])

Fig. 4.—Donor site, once healed, but now ulcerated as a consequence of increasingly poor nutrition (Courtesy of Levenson and Lund.[63])

Levenson and co-workers[60] have studied extensively the healing of thermal burns in human beings. They observed that while there was no significant difference in the rate of sloughing of the dead tissue in protein-deficient individuals as compared with nondeficients, there was a marked delay in wound closure in the former group. In such patients granulations were often soggy, edematous, and friable or, in occasional cases, absent (Fig. 3). Local exudation and injection were increased. Epithelization from the periphery, or from pin-point grafts, was markedly delayed or completely inhibited. This delay in epitheliza-

tion was apparently a more sensitive indication of deficiency than the taking of grafts, since some patients were observed in whom sheet grafts and pin-point grafts "took," but in whom subsequent epithelization of either the burned area or the donor sites failed. It was also observed that successful skin grafts and healed donor sites "broke down" in patients who had subsequently become markedly protein deficient (Fig. 4).

It is well recognized that significant infection slows the healing of wounds. This is true not only for infections of the wounds themselves, but also for infections elsewhere in the body. It has been recently stressed, particularly by Cannon and his co-workers,[16] that the protein-deficient animal is less resistant to infection than "the normal." Cannon has pointed out that both natural and acquired resistance are probably affected by the state of protein nutrition, since the elements involved in resistance (such as phagocytes and antibodies) are protein in nature and their production may be influenced by the same factors which influence the production of other body proteins.

During the past few years there has been considerable interest in, and study of, the metabolic abnormalities following acute trauma.[1, 34, 60] An increased urinary excretion of nitrogenous products following injury, particularly fractures and major burns, major operations, and serious acute illnesses, has been demonstrated by many investigators. This increased nitrogen excretion begins very shortly after the onset of the illness, reaches its peak during the first week, and persists for two to six weeks. By and large, the intensity and duration of the "catabolic reaction" parallels the severity of the injury. This reaction is exhibited markedly by previously well-nourished adult males and to a lesser extent by females and children. It is not seen in previously malnourished individuals. The mechanism of the extensive nitrogen excretion is not fully understood, but it is probable that there is more than one precipitating factor. The healing of wounds during the early catabolic phase has not been adequately studied.

Ascorbic Acid

It has been long known that wound healing is impaired in scurvy. Many descriptions of scurvy in sailors in the middle eighteenth century include statements such as, "The whole body, and more especially the legs, were subject to ulcers of the worst kind attended with rotten bones and such a luxuriancy of fungous flesh as yielded to no remedy."[30]

For much of our present knowledge of the role of vitamin C in wound healing we are indebted to the pioneering research of Wolbach and Bessey.[96, 97, 98] They showed that the morphologic consequences of experimental ascorbic acid deficiency are practically restricted to supporting tissues of mesenchymal origin and may be expressed by the statement that there is failure of formation and maintenance of intercellular materials. This definite and simple characterization explains the pathology of experimental ascorbic acid deficiency in susceptible animals and in the naturally occurring deficiency in man (scurvy).

It is believed that ascorbic acid is not necessary for the survival and multiplication of the cells concerned with matrix formation. The deficiency is specifically concerned with the elaboration of intercellular substance, which is regarded as the product of cells.

The mechanism by which ascorbic acid promotes the formation of collagenous intercellular substances is not known. It may be involved in the chemical mechanisms (enzymes) of the cells responsible for the synthesis of this protein product, collagen. The hypothesis that ascorbic acid or a derivative is part of the collagen structure cannot be excluded on the basis of present knowledge.

New capillary formation is prevented by severe ascorbic acid depletion. Islands of hematopoiesis form adjacent to abortive capillary formations in the neighborhood of spontaneous hemorrhages or in the tissue surrounding blood clots after excision of muscle, in severe ascorbic acid depletion. The source of the blood-forming cells awaits demonstration, but the inference has been made that they are derived from endothelial cells which accumulate in consequence of failure of capillary formation.

It is agreed that vitamin C deficient guinea pigs exhibit impaired incisional wound healing both histologically and in terms of tensile strength. In completely or partially deficient animals the tensile strength of healing wounds lags behind that of controls, the degree being roughly proportional to the extent of the deficiency.[13]

The time required for the tensile strength to reach a maximum in partially scorbutic animals was also found in most investigations to be prolonged, although Taffel and Harvey[87] stated that wound strength in partially deficient animals approached the normal at twelve to fourteen days. Hartzell and Stone,[36] on the other hand, noted a marked decrease in the strength of wounds in partially deficient animals throughout the fourteen-day period of the experiment, and Lanman and Ingalls[59] found subnormal strength in test animals as late as thirty days postoperatively. In addition to the impaired tensile strength in vitamin C deficient animals, there is evidence that such animals are more susceptible to wound infection and that infection, when present, is apt to be of a spreading type in the scorbutic as compared to the normal control. Histologic studies of experimental abscesses in guinea pigs have revealed less localization and more diffusion of the inflammatory reaction and infecting organisms in the scorbutic animals, as compared to the controls.[74] In addition, Bartlett and associates[7, 8] found that when virulent organisms were injected at a point distant from the operated wound, the same organism was later found at the operative site in a definite percentage of scorbutic animals.

Bourne[13] studied in detail the relationship between vitamin C intake, plasma vitamin C level, and tensile strength of healing incisions in guinea pigs. He found that in the low intake range there was a parallelism between these factors. However, an intake greater than that necessary to avert scurvy did not result in any increase in tensile strength, although the animal was more nearly "saturated" with vitamin C. This was confirmed by Bartlett. Thus, although the daily administration of 15 to 30 mg. of ascorbic acid to the guinea pig will pro-

duce an elevation in both scar tissue and plasma vitamin C levels (and presumably in vitamin C excretions), the wound tensile strength in animals so treated is no greater than that of similar wounds in animals given 1.5 to 2.0 mg. daily. There is some evidence, however, that saturation levels of vitamin C aid the animal in resisting the violence and severity of wound infection. Jones and co-workers[52] found that when wounds were intentionally inoculated with virulent organisms, the resultant infection and mortality was definitely greater not only in the scorbutics as compared to the normal controls, but was greater in these latter as compared with a group of animals receiving "saturation doses" of vitamin C.

Bourne[13] cited the observations of Lauber and Rosenfeld[57] that vitamin C is apparently mobilized from the organs of a wounded scorbutic animal and selectively concentrated in the traumatized area. Bartlett, Jones, and Ryan[7, 8] also found a relatively high concentration of vitamin C in the newly formed scars of normal controls and deficients. In deficient animals the concentration of vitamin C in the scar, although low, was greater than that in the abdominal wall immediately adjacent, suggesting a preferential concentration at the site of trauma. In this regard, Bartlett and co-workers[8] have shown that vitamin C given postoperatively, beginning at the time of operation, to deficient animals and man (one case) will result in satisfactory wound healing.

The importance of vitamin C in the physiology of wound healing is substantiated by the histologic studies of many workers. Hunt[50] has followed the healing of incisional wounds in normal and partially scorbutic animals and has noted delay in the formation of precollagen and an absence of maturation of precollagen (Fig. 5, *A* and *B*). Cellular proliferation was delayed, but once started it extended throughout the entire experimental period of three weeks. However, maturation of the fibroblasts was delayed. While the scars of normal animals consisted of mature fibrocytes in a matrix of collagen after fourteen days, those of deficient animals were composed of fibroblasts in a precollagenous matrix. In common with earlier workers he noted that vascularization did not proceed normally in the deficient group so that the resultant scars appeared puckered, discolored, hemorrhagic, and indurated. Lastly, he noted the reversion of apparently mature collagen to the precollagenous state in the wound of a previously normal animal placed on a scorbutic diet twenty-one days postoperatively. This is in keeping with older observations of the breaking down of wounds long healed when scurvy appeared.

Although, as mentioned, impaired wound healing in man has long been associated with scurvy, it is only relatively recently that the problem has systematically been studied in man. Lanman and Ingalls[59] reported a case of wound rupture and death in an infant, the findings at autopsy suggesting scurvy. Archer,[6] in 1936, suggested that the scorbutic state may predispose to poor healing and leakage of operative anastomoses in the human being. The pioneer experimental observations on controlled vitamin C deficiency in an otherwise normal human being were made by Crandon and Lund.[24, 25, 69] Crandon was maintained on a diet free of ascorbic acid but otherwise complete for a

period of about six months. Forty-two days after the start of this diet the plasma vitamin C level had reached zero, but the white blood cell ascorbic acid did not sink to this level until 122 days. An experimental wound (two inches in length) made three months after the start of the experiment appeared to heal normally, the criteria used being those of gross and histologic appearances on biopsy. Tensile strength measurements were not made. The patient at this time was clinically well except for a moderate loss of weight and drop in basal

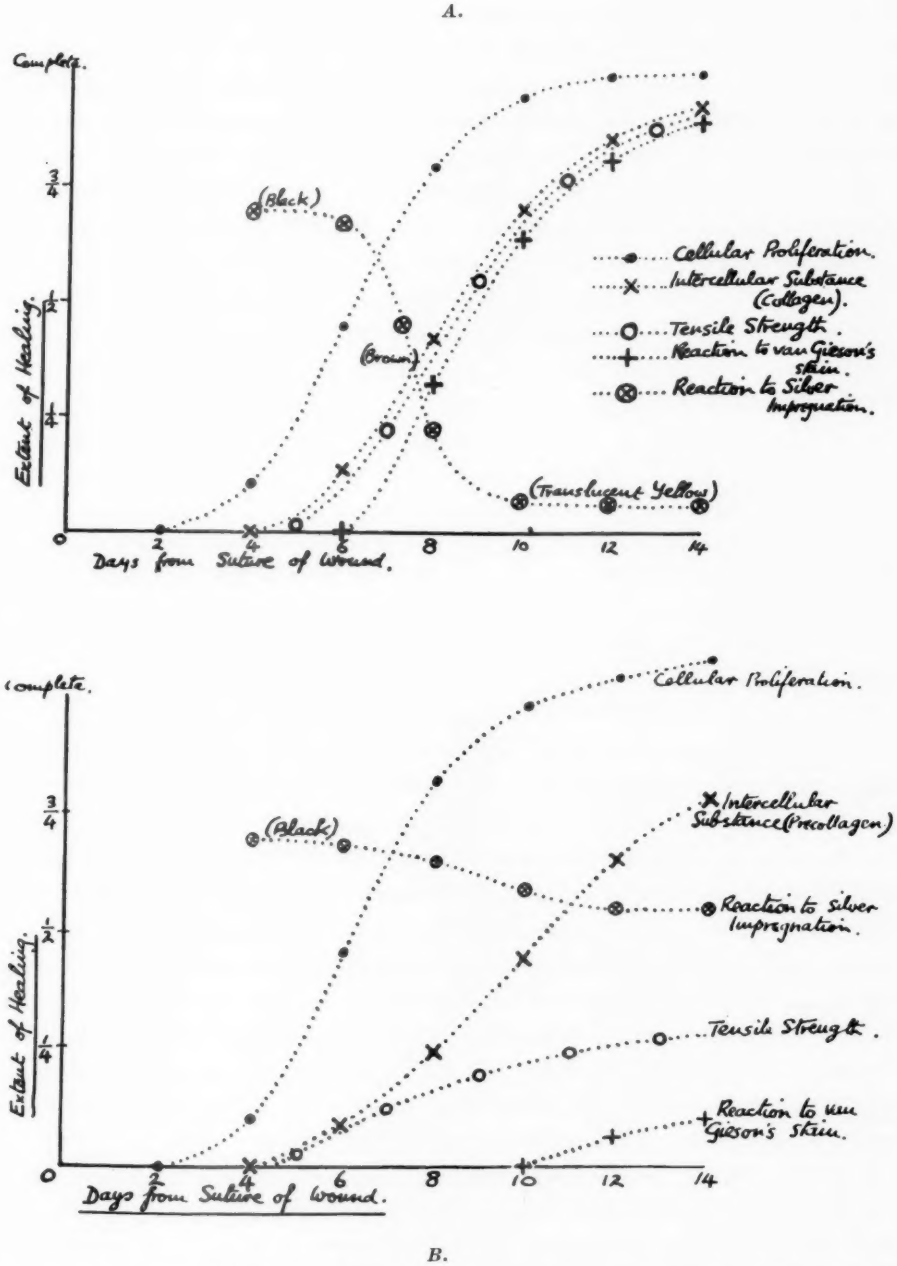

Fig. 5, *A* and *B*.—Graphs illustrating in a semiquantitative manner the course of wound healing as judged by the staining reactions of intercellular substance in wounds of guinea pigs. *A*, normal guinea pigs. *B*, subscorbutic guinea pigs. (From Hunt,[50] Brit. J. Surg.)

metabolic rate. At 161 days petechiae were noted on the limbs, and a second wound, similar to the first, made at the end of six months revealed faulty healing as evidenced by gross failure of the wound edges to unite below the skin. A lack of formation of intercellular substance and vascular elements was apparent on histologic examination of a ten-day biopsy specimen of the wound. After this biopsy the subject was given a daily supplement of 1,000 mg. of ascorbic acid. A second biopsy ten days later revealed "... good healing, the sections showing ample intercellular substance and capillary formation."

Crandon and Lund's findings have been corroborated by the work of others. Wolfer and associates[99] noted that the efficiency of wound healing in experimental vitamin C deficient human subjects as estimated by tensile strength measurements, as well as histologic appearance, was markedly impaired. When circumstances for healing are poor, as in cases with undue wound tension or diminution of blood supply, the ascorbic acid depletion is made even more evident through gross failure of primary wound healing. The incidence of wound infection under such circumstances suggests the need for ascorbic acid in the tissues for maximal resistance to infection. This is in keeping with the observations of Bartlett and co-workers already described.

Bartlett, Jones, and Ryan[8] have shown in one case of a two-stage bilateral herniorrhaphy that human wound healing, as measured by tensile strength determinations, is inferior in the presence of plasma and tissue vitamin C depletion, and that normal healing can be induced in a depleted patient by adequate postoperative oral vitamin C administration (1,000 mg. daily for ten days). This is in agreement with previous observations made by these workers and by Hartzell and Stone[36] on the efficacy of postoperative administration of ascorbic acid to previously deficient experimental animals.

There have been many reports in the literature indicating that a high percentage of surgical patients with serious illnesses enter the hospital with relatively low plasma vitamin C levels, and it had been inferred that such patients were deficient in vitamin C and thus, presumably, would have impaired wound healing. The observations in this regard were equivocal. However, it is now recognized that the interpretation of plasma vitamin C concentration is difficult, and a low plasma concentration per se does not necessarily indicate tissue vitamin C deficiency. More careful and controlled observations are needed.

Recently, interest has been aroused in the abnormalities of vitamin C metabolism following acute trauma.[4, 5, 83, 90] Levenson and associates[61, 70] demonstrated a fall in plasma ascorbic acid concentration, a decrease in urinary ascorbic acid excretion, and a decreased response to "load" tests. The extent of the change roughly paralleled the extent of injury. In some instances the patients, previously well and in good nutritional state, were "biochemically scorbutics." It would be of interest to determine whether or not such patients are also "physiologically scorbutics," that is, in the healing of wounds. Preliminary observations suggest that this may be the case. Similar biochemical abnormalities in the metabolism of thiamine, nicotinamide, and riboflavin were noted. Andreae and associates[4, 5] also reported similar findings.

Vitamins A and D

For many years cod-liver oil has been applied locally to open wounds. Although it has been observed that vitamin A deficient animals exhibit delayed repair and an increased incidence of wound infection,[14] there is no good evidence that the administration of vitamins A and D in any form (topically or otherwise) affects the healing process in animals with no deficiencies of these essentials. Most clinical reports[31, 33, 68, 77] have, however, been enthusiastic as to their efficacy when used locally in this manner on granulating wounds. There are, on the other hand, some studies, such as the apparently well-controlled work of Brush and Lam,[15] which indicate that there is no specific therapeutic effect attributable to cod-liver oil in the absence of definite vitamin A deficiency. Moreover, there is lack of unanimity of opinion as to the nature of the possibly therapeutically active factor in cod-liver oil, although in general this has been identified with the nonsaponifiable fraction, and it is in this fraction that vitamins A and D are found.[31] A number of authors feel that the growth-promoting activity, while accumulating in the vitamin-containing fraction, is not attributable to the vitamin content. Others have felt that the proportion of vitamins A and D was important.[68] All in all, the issue is confusing and there are really very few good reports on the influence of vitamin A on wound healing.

Lauber[57a] reported studies on rats 10 or 12 weeks of age with surface wounds 2 by 2 cm. on their backs. There was no effect of vitamin A given prior to operation in normal animals. However, in normal animals in whom the vitamin A administration was begun at the time of operation, there was acceleration of wound healing when 4 units per day were given; no effect was noted when 200 units were given, and retardation followed when 40,000 units were employed. Younger animals appeared to be more sensitive than adults to vitamin A toxicity. Similar retardation of wound healing by large doses of vitamin D was also described by Lauber.

Brandaleone[14] reported no increase in the healing rate of surface wounds in normal rats treated topically with cod-liver oil. However, in vitamin A deficient animals marked benefit resulted from treatment with cod-liver oil by oral or topical routes. While oral administration proved the more effective in relieving systemic evidence of vitamin A deficiency, topical application had a greater accelerating effect upon the specific process of wound healing. That the administration of vitamin A to an animal deficient in this factor should benefit several physiologic processes, wound healing included, is not surprising. However, the mechanism of impaired wound healing in vitamin A deficient rats must be re-evaluated in view of the recent findings of vitamin C deficiency in such animals. There is no good evidence to indicate that the administration of vitamins A and D to nondeficient animals is of any benefit. There are no studies reported to date on the effect of acute illness and trauma on the metabolism of the fat-soluble vitamins such as those already mentioned in relationship to the water-soluble vitamins.

Vitamin B Complex

In contrast to the many studies on the relationship of ascorbic acid to the healing of wounds there are relatively few studies of a comparable nature in regard to the B complex vitamins. Recently Bosse and Axelrod[12] reported on the healing of surface wounds in riboflavin-, pyridoxine-, and biotin-deficient animals. In this study the rats were placed on the appropriate diet, either control or experimental, for a period of five weeks, after which circular excisions of skin 13 mm. in diameter were made. The wounds were then excised at three, six, fourteen, and twenty days postoperatively for histologic examination, and, in addition, gross observations as to healing rates were made. These workers report that the healing of wounds in the pyridoxine- and riboflavin-deficient animals was markedly delayed, the controls healing in fourteen days and the experimentals in twenty days. No such retardation was noted in the biotin-deficient animals. Histologic examination of wounds on the third, sixth, and fourteenth postoperative days in the biotin-deficient animals, however, revealed some retardation in collagen production and in density of the granulation tissue, while the amount of precollagen and the vascularity was greater than in the normals. At twenty days the histologic appearance of the wounds in the biotin-deficient animals was indistinguishable from that of the controls. In contrast, the pyridoxine- and riboflavin-deficient animals exhibited much greater differences from the normals. There was a marked delay in initial contraction of the wounds, a delay in epithelization, and an apparent decrease in the amount of collagen with a considerable admixture of precollagen. The latter, in fact, was observed in these experimental wounds at a time when it was absent in the control and biotin-deficient groups. Scar tissue in the pyridoxine- and riboflavin-deficient animals was less dense, more vascular, and more cellular than in the normals. Such abnormalities were more marked in the pyridoxine-deficient group.

In evaluating these results, as the authors pointed out, the possible role of inanition must be considered. Both the pyridoxine- and riboflavin-deficient animals had lost considerable amounts of weight as compared to the normal and biotin-deficient animals. However, Bosse and Axelrod pointed out that the riboflavin-deficient group had lost the most weight, whereas the pyridoxine-deficient animals showed the most marked delay in the healing of the wounds. It would appear, then, that perhaps there is a specific influence of pyridoxine and possibly riboflavin on the healing of surface wounds. However, other studies in which the factor of inanition is controlled are required before any definite conclusion can be reached. There are no significant clinical studies reported in which the role of the B complex group in the healing of wounds is elucidated.

Carbohydrates

There are very few studies available as to the role of carbohydrates in the healing of wounds. It is recognized clinically that uncontrolled diabetics show interference in the healing of wounds. However, what specific factors are responsible for this cannot be stated at present. There is little experimental evidence on the course of wound healing in diabetic animals. However, one such

study on dogs made diabetic by pancreatectomy indicates some interference in the healing of abdominal wounds. More work is needed before the specific role of carbohydrates in the healing of wounds can be adequately evaluated.

Dehydration

Little work has been reported on the specific effects of dehydration on the healing process. Bird and McKay[11] induced dehydration through simple water deprivation pre- and postoperatively in both starving and adequately fed animals. The tensile strength of stomach incisions was measured by techniques similar to that of Harvey and Howes. Significant diminution in the mean tensile strength of healing stomach wounds was found in both dehydrated groups, as compared with similar controls in each case. In addition, a weakening of the stomach wall as a whole was noted in the dehydrated groups (Fig. 6). Sandblom[82] also reported a deleterious effect of dehydration on the healing of incisional wounds in rabbits, both normal and anemic.

Other Nutritional Factors

It is probable that other nutritional factors may play a part in the healing of wounds. However, no studies are at present available to assay the importance of such factors in this process.

ANEMIA

Despite the fact that frequent reference has been made in clinical articles to the supposed adverse effect of anemia on the healing process,[44, 93-95] there are actually very few studies of this problem, and no conclusive evidence has been found by us to support this supposition. Levenson, Maloney, and Lund,[63] surveying the healing of second degree burns in children, had the impression that there was no difference in the rate of healing in patients with moderate anemia as compared to those with normal hemoglobin levels. Besser and Ehrenhaft[9] investigated the effects of acute anemia on the healing of stomach wounds in dogs. Just prior to operation an acute anemia (hemoglobin concentrations of about 50 per cent) was produced by femoral venesection with immediate replacement of the lost plasma from pooled donor sources. Care was exercised to prevent any deficiencies other than the anemia, and there was no significant change in the plasma protein concentration. The experiment was carried on for eleven days postoperatively, by which time the experimental animals had recovered from their anemia. The authors stated that "The mean values of the tensile strengths of the incisions in the anemic and control dogs showed no significant differences." Histologic study also failed to reveal variations in the two groups.

In contrast, Sandblom[82] produced an acute anemia (mean hemoglobin 35 per cent) without hypoproteinemia in rabbits by bleeding them from the carotid artery, and noted a mean reduction of 39.2 per cent in the tensile strength of healing dorsal skin incisions on the fifth postoperative day in the presence of anemia when compared to the control values—a difference which is statistically significant. No observations were made on days other than the fifth.

Sako and co-workers,[81] also working with rabbits made acutely or chronically anemic by venesection, noted a decreased tensile strength on the seventh postoperative day in healing abdominal incisional wounds. They were able to bring about normal healing in these animals by transfusion of either fresh or banked blood at or immediately following operation.

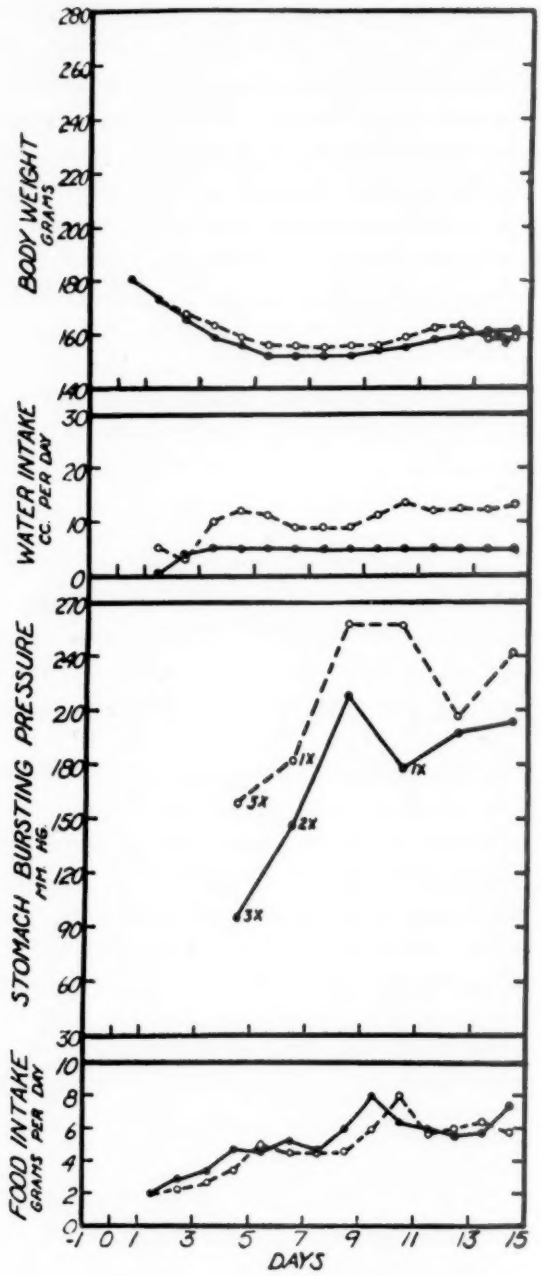

Fig. 6—Effect of chronic dehydration on the tensile strength of stomach wounds in rats. (From Bird and McKay,[11] Surg., Gynec. & Obst.)

Waterman, Birkhill, and Levenson[91] found that nutritional milk anemia of severe degree (about 6 Gm. hemoglobin per 100 ml. blood) maintained for from two to six weeks prior to operation in the albino rat has no effect, deleterious or otherwise, on the healing curves, total healing times, and histologic appearances of open operative skin wounds (Fig. 7).

There are several possible explanations for the discrepancies noted in regard to the effect of anemia on wound healing. Waterman and co-workers studied the healing of open wounds in albino rats, while both Sandblom and Sako followed the healing of sutured incisions in rabbits. Further, Sandblom and Sako and associates made observations at only one point on the healing curve, whereas the entire curve of healing was followed in Waterman's study. The fact that these discrepancies are present serves as a warning against indiscriminate application of data obtained in one species of animal to other species or to man, and argues against the assumption that factors operative in the healing of one type of wound necessarily apply to the healing of wounds of a different type.

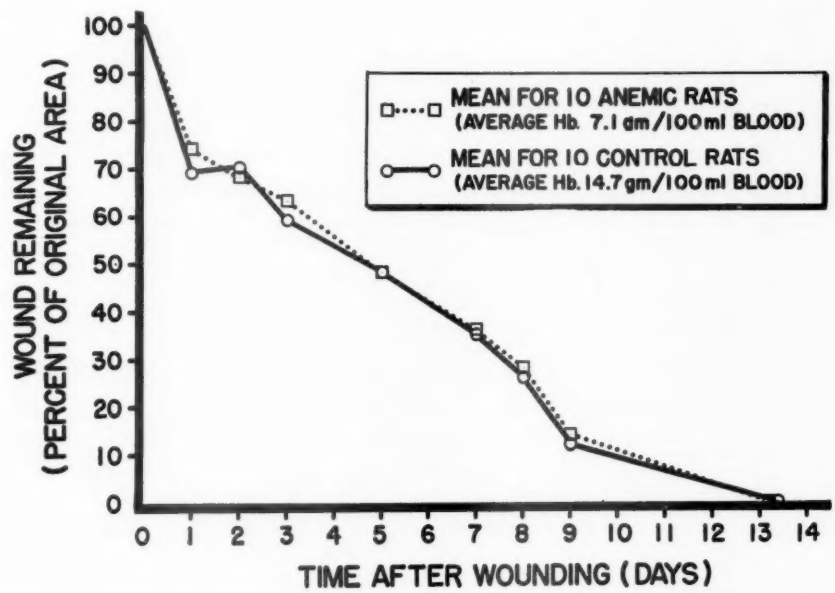

Fig. 7.—Healing curves of surface wounds in albino rats. Controls are compared with rats made anemic on a milk diet.

It is also possible that anemia more severe, both in regard to degree and duration, might have some deleterious effect on the healing of wounds. This, however, has not yet been investigated. The additional possibilities that the use of larger wounds or the presence of other deficiencies in addition to anemia might result in impaired wound healing should also be considered.

AGE

It is well recognized that wounds heal at a faster rate in young individuals as compared to wounds in older individuals. We have previously pointed out

that Du Nouy[26, 27, 28] formulated a mathematical expression for the course of the healing of open wounds in man in which an index of cicatrization "i," a constant characterizing each wound, was found, this constant being larger the younger the patient. Carrel and Du Nouy theorized that this might be due to either a growth-promoting substance in the younger individuals or a growth-retarding substance in the older individuals. Carrel and Ebeling[19] investigated the effect of serum from animals of different ages on fibroblastic proliferation in tissue culture. He demonstrated that there was no stimulating factor present in the serum from young animals, but that there was evidence of a restraining power of adult serum on cell multiplication (Fig. 8). Carrel[17] felt that the inhibiting factor was associated with the lipoid fraction.

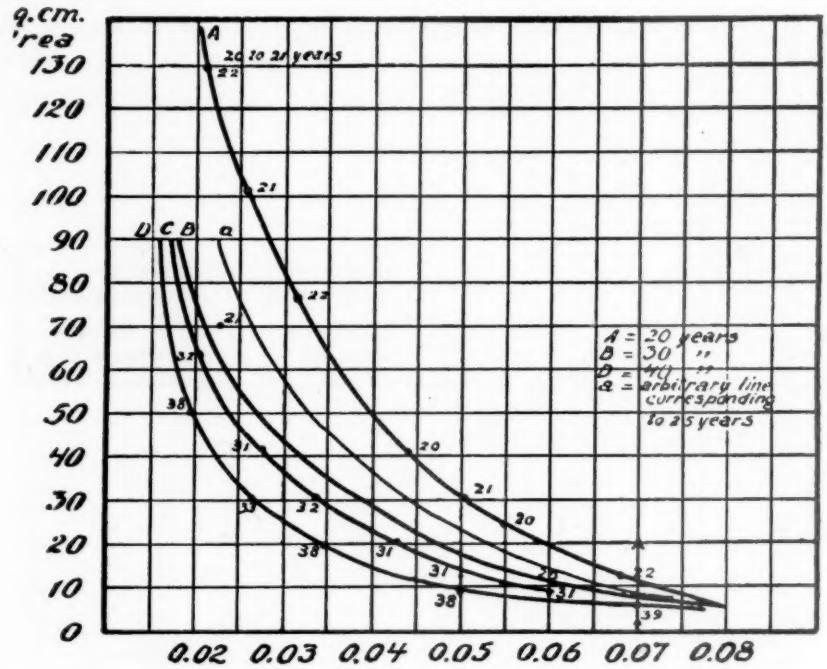

Fig. 8.—Healing curves of surface wounds in men of different ages. (From Du Nouy,[26-28] J. Exper. Med.)

Howes and Harvey[47] have also demonstrated the influence of age on wound healing. They state that in the rat the lag period is shorter in the young, and tends to lengthen with age. Fibroplasia began one day earlier in young rats as measured by tensile strength and also by microscopic examination. In spite of the earlier beginning the rate was no greater in the young than in adults, the slope of the curve being parallel during the fourth, fifth, and sixth days. However, the period of accelerated fibroplasia was of longer duration in the young, lasting through the period from the third to seventh days, in contrast to its duration in adults, which was restricted to the period from the fourth to sixth days. It appears, therefore, that the shortening of healing time of wounds of young animals depends on the diminution of the amount of retardation entering into the process, rather than an actual increase in the rate of fibroplasia. These studies tend to confirm those of Carrel.

Clinically it is generally held that children's wounds heal faster than those of adults. In an extensive study of thermal burns in human beings, Levenson, Maloney, and Lund[63] observed that second degree burns heal consistently faster in infants and children than in adults, and that, in general, grafts "take" better in younger patients.[62]

COMMENT

A critical review of the effects of nutrition, anemia, and age on the healing of soft tissue wounds was undertaken as a preliminary to experimental studies contemplated in this laboratory. The literature on these subjects was found to be incomplete and controversial. In many studies fundamental considerations such as accurate and consistent definitions, suitable and adequate controls, and statistical analyses of the results have been neglected. It is essential that these fundamentals of experimental physiology be considered in future studies, since the process of wound healing is complex, and, as presently measured, shows very marked individual variations. Further, there has been a tendency to consider automatically the results observed in the healing of wounds in one species of animals as applicable to the healing of wounds in another species. In addition, the processes in the healing of different types of wounds, such as superficial ulcers and deep incisional wounds, have been equated without question. Although these processes have certain features in common, there is no assurance, at present, that laws, descriptions, and formulas found applicable in the one instance are necessarily applicable in the other.

In the text, after preliminary discussions of definitions, descriptions, techniques of measurement, and interpretations of wound-healing processes, the reported studies on the effects of the following on the healing of soft tissue wounds are systematically appraised: short-term high protein, high fat, or high carbohydrate diet in animals; acute and chronic protein deficiency in experimental animals and in man; plasma, acacia, and methionine therapy in chronically protein-deficient animals; ascorbic acid deficiency in animals and in man; vitamins A, D, biotin, pyridoxine, and riboflavin deficiencies in animals; diabetes; dehydration; anemia; and age.

It is fruitless to attempt to summarize the reported studies since full consideration of the experimental conditions and techniques is necessary for critical evaluation. It is sufficient to indicate that considerably more carefully controlled experimental and clinical studies are required before definite conclusions can be drawn about the effects and mechanisms of action of nutrition, anemia, and age on the healing of soft tissue wounds.

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Book Reviews

Textbook of Anaesthetics. By R. J. Minnitt, M.D. (Liverpool), D.A., R.C.P. & S. (Eng.), Trinity College, Cambridge, and John Gillies, M.C., M.B., Ch.B. (Edin.), F.R.C.S. (Edin.), D.A. (Eng.). Baltimore, 1948, Williams & Wilkins Company.

The entire field of anesthesia has been covered in a brief and concise manner. Most of the illustrations are good and add to the reader's interest. The book is suitable not only for a beginner in anesthesia but should be a useful guide as well for the general practitioner who must do anesthesia.

On the whole, the theories and concepts of anesthesia practice are sound. One can, however, question details such as the following: In the chapter on nitrous oxide the authors appear to condone severe anoxia; further, they describe signs of nitrous oxide anesthesia which are in fact the signs of anoxia. To use cyanosis as a guide in anesthesia is courting disaster. An anoxic technique for the administration of ethylene is also described. In the treatment of convulsions during anesthesia the suggestion of Coramine is surely open to question. The danger of ventricular fibrillation occurring with ethyl chloride administration has not been mentioned in the chapter dealing with this drug.

The authors have well stated that chloroform should be used only if no other form of anesthesia is applicable. The judicious use of endotracheal tubes by the oral route is to be commended. The use of picrotoxin or Coramine mixed with intravenous barbiturates has not proved to be of value.

In the treatment of cardiac arrest (syncope), massage of the heart has been listed as the last resort. If delayed until the other measures described have been used the patient will either have recovered spontaneously or will be dead.

The section on oxygen therapy is brief but the criteria of successful oxygen therapy have been well stated. The section on regional anesthesia is much improved over the previous edition, with better illustrations and improvement in the text.

Fundamental Considerations in Anesthesia. By Charles L. Burstein, M.D. Pp. 153. New York, 1949, The Macmillan Company.

This short book, one discovers, deals primarily with the nervous system, although its title would imply a broader interest. There is a considerable lack of uniformity in the degree of detail presented in the fifteen chapters. For example, the first chapter is concerned with the autonomic nervous system. It is disposed of in about four pages, while three times this much space is given to a discussion of laryngeal spasm. This example points up the author's emphasis on the abnormal rather than on the normal.

The order of the chapters is somewhat surprising. A chapter on traumatic shock is interposed between the chapter on laryngeal spasm and one on the celiac plexus reflex. The material in the chapter on shock might have been prepared a decade or two ago, judging from the references to "toxins," to "increased capillary permeability," to hemoconcentration as a sign, to "sympathetic overactivity," and so on.

It is not clear who would find this book useful. Too little attention is given to normal physiologic or pharmacologic material to make this a satisfactory treatise for the neophyte. The considerable number of inaccuracies is a further drawback. The discussion of most of the subjects is too superficial to interest the expert.

Medullary Nailing of Kuntscher. By Lorenz Böhler. First English edition, Pp. 386, with illustrations. Baltimore, Md., 1948, Williams & Wilkins Company. $7.

Böhler is uniquely equipped to evaluate a new method of treating fractures because of his past experience and continuing wealth of clinical material. Rigid standardization in treatment, coupled with exact follow-up records, provide the background for this report upon the use of the Küntscher intramedullary nail in the treatment of diaphyseal fractures. His general conclusions are of special interest: (1) Intramedullary nailing is not an emergency procedure and should be performed only under optimal conditions. (2) Such operations should be performed by surgeons trained in the treatment of fractures and only when an adequate armamentarium is available. (3) Fracture healing is somewhat delayed by intramedullary nailing. (4) Complications are frequent and are due to errors of the surgeons rather than to an intrinsic fault in the method. (5) Closed reduction and nailing, in contrast to open operation upon the fracture site, is the treatment of choice because it minimizes the dangers of infection. It is only with this last conclusion that most American surgeons will differ, preferring to open the site of fracture rather than to attempt a difficult, complicated, and often prolonged reduction using cumbersome apparatus and requiring frequent roentgenograms. Bohler describes the technique for nailing all long bones, but recommends the method as the procedure of choice only in fractures of the shaft of the femur. The role of intramedullary fixation in reconstructive bone operations is discussed. No surgeon assaying this method of fracture treatment should proceed without careful perusal of this excellent monograph.

Neuro-Radiology. By Alexander Orley, M.D., F.F.R., D.M.R. & E. Honorable Consulting Radiologist, West End Hospital for Nervous Diseases, London. Pp. 421. Springfield, Ill., 1949. Charles C Thomas, Publisher.

This edition is said to have little in common with the original Wakely and Orley textbook of neuroradiology published in 1938.

The first forty-eight pages are devoted to the technique of radiography of the skull. This section is well illustrated by good photographs and drawings.

This book is, for the most part, a concise treatise on those features of neuroradiology constantly encountered by the neuroradiologist. Cerebral angiography is done with Thorotrast through exposure of the arteries. In this country this has been almost universally abandoned and percutaneous injection of Diodrast has supplanted it. The discussion of angiograms is very elementary. Iodized oil after myelography, when removed at all, is removed at subsequent operation or through a trephine hole in the sacrum. This also is an obsolete procedure in this country, where the oil is aspirated through the spinal puncture needle when the examination is completed.

Many of the roentgenogram reproductions are so small that one cannot recognize the features alluded to in the text.

The author repeatedly uses an unexplained abbreviation (G. P. I.) in the text and even in the index. It is irritating to the reader to encounter such unclear, unexplained letter combinations, which perhaps are localisms.

There is a more extensive bibliography than one would expect from the contents of the book. There are 843 references at the end of the book arranged according to subject matter.

The general radiologist and the neurologist will find much valuable material in this book.

Pediatric Anesthesia. By M. Digby Leigh, M.D., and M. K. Belton, M.D. Pp. 240. New York, 1948. The Macmillan Company.

This book presents a long-needed exposition of a field in anesthesia with which few have had extensive enough personal experience to become well versed. Those who have had

intensive pediatric practice seem to agree that expert proficiency in it requires great concentration of training and experience, and this, Dr. Leigh has had.

In a clear, readable fashion Dr. Leigh here sets down his personal observations and opinions on the conduct of anesthesia for children, with due emphasis to the meticulous care required in all aspects of the work. Application of "adult" methods, such as spinal, pentothal, curare, and endotracheal intubation in the hands of skilled individuals will surprise many. Much that many general hospitals tend to overlook in anesthetic management of children is emphasized: psychology of handling patients, premedication, body temperature changes, fluid therapy.

Although more objective data would be desirable, this brief volume serves as a welcome clinical guide. It should help to dispel that veil of metaphysical explanations (for example, "status thymicolymphaticus") for bad anesthesia, and for sudden unexplained catastrophes in infants.

Books Received

The receipt of books is acknowledged in this section and this treatment must be regarded as sufficient acknowledgment of the courtesy of the senders. Selections will be made for more extensive review dictated by the interests of our readers as space permits.

LEHRBUCH DER RONTGENDIAGNOSTIK. By H. R. Schinz, W. E. Baensch, E. Friedl, and E. Uehlinger. Paper. Pp. 426, with 507 illustrations. Stuttgart, 1950, Georg Thieme verlag.

DIE GYNAKOLOGISCHEN OPERATIONEN. By Prof. Dr. Med. Heinrich Mhrtius, Direktor der Universitats Frauenklinik Gottingen. Hard. Pp. 436, with 422 illustrations. Stuttgart, 1950, Georg Thieme verlag.

WATER AND SALT DEPLETION. By H. L. Marriott, C.B.E., M.D., F.R.C.P., Middlesex Hospital, London, England. Soft (imitation leather). Price $2.00. Pp. 80, with no illustrations. Springfield, Ill., 1950, Charles C Thomas, Publisher.

CLINICAL NUTRITION. Edited by Norman Jolliffe, M.D., F. F. Tisdall, M.D., and Paul R. Cannon, M.D., for Food and Nutrition Board of National Research Council. Hard. Price $12.00. Pp. 925, with 127 illustrations and 78 tables. New York, 1950, Paul B. Hoeber, Inc.

MORBUS CAERULEUS, AN ANALYSIS OF 114 CASES OF CONGENITAL HEART DISEASE WITH CYANOSIS. By S. Eek, M.L., and others, The Crown Princess Lovisa's Children's Hospital, Stockholm, Sweden. Hard. Price $9.25. Special edition. Pp. 332, with 122 illustrations. Basel and New York, 1949, S. Karger.

CLINICAL USES OF INTRAVENOUS PROCAINE. By David J. Graubard, M.D., and Milton C. Peterson, M.D., New York Post-Graduate Medical School and Hospital, New York, N. Y. Soft. Price $2.25. Pp. 104, with some illustrations. Springfield, Ill., 1950, Charles C Thomas, Publisher.

ANXIETY IN PREGNANCY AND CHILDBIRTH. By Henriette R. Klein, M.D., Associate in Psychiatry, Columbia University College of Physicians and Surgeons, New York, N. Y.; Howard W. Potter, M.D., Professor of Psychiatry, Long Island College of

Medicine, Brooklyn, N. Y.; and Ruth B. Dyk, M.S., Research Department, New York City Youth Board. Hard. Price $2.75. Pp. 111, with some illustrations. New York, Paul B. Hoeber, Inc.

MODERN TRENDS IN ORTHOPAEDICS. By Sir Henry Platt, M.D., M.S., F.R.C.S., Professor of Orthopaedic Surgery, University of Manchester. Hard. Price $10.00. Pp. 497, with 222 illustrations. New York, Paul B. Hoeber, Inc.

PROCTOLOGY IN GENERAL PRACTICE. By J. Peerman Nesselrod, B.S., M.S., M.Sc., M.D., F.A.C.S., F.A.P.S., Associate in Surgery, Northwestern Medical School. Hard. Pp. 276, with many illustrations. Philadelphia, 1950, W. B. Saunders Company.

THE GENEALOGY OF GYNAECOLOGY. By James V. Ricci, A.B., M.D., Department of Gynaecology and Obstetrics, New York Medical College, City Hospital Division, New York, N. Y. Hard. Price $8.50. 2. Ed. Pp. 494, with no illustrations. Philadelphia, 1950, The Blakiston Company.

PATHOLOGY IN GENERAL SURGERY. By Paul W. Schafer, M.D., Professor of Surgery, University of Kansas School of Medicine. Hard. Price $17.50. Pp. 581, with many illustrations. Chicago, 1950, University of Chicago Press.

BRITISH SURGICAL PRACTICE. VOL. 7, PHARYNGEAL DIVERTICULA TO SPINAL CORD. By Sir Ernest Rock Carling, F.R.C.S., F.R.C.P., Westminster Hospital, and Sir James Paterson Ross, K.C.V.O., M.S., F.R.C.S., Professor of Surgery, University of London. Hard. Pp. 591, with 339 illustrations. St. Louis, Mo., 1950, The C. V. Mosby Company.

THE MERCK MANUAL. By Merck and Company, Inc. Hard. Price $5.00. 8 Ed. Pp. 1592. Rahway, N. J., 1950, Merck and Company, Inc.

ANNUAL REVIEW OF MEDICINE. Vol. I. Dr. Windsor C. Cutting, editor, and Dr. Henry W. Newman, associate editor. Stanford University School of Medicine. Hard. Price $6.00. Pp. 484, with no illustrations. Stanford, Calif., 1950, Annual Reviews, Inc.

PEPTIC ULCER. By A. C. Ivy, Ph.D., M.D., D.Sc., LL.D., Vice President of the University of Illinois in charge of Chicago Professional Colleges; M. I. Grossman, Ph.D., M.D., Associate Professor of Physiology in The Department of Clinical Science, University of Illinois College of Medicine; and William H. Bachrach, Ph.D., M.D., Research Associate in Physiology, University of Southern California School of Medicine. Hard. Price $14.00. Pp. 1,144, with 137 illustrations. Philadelphia, 1950, The Blakiston Company.

TRANSACTIONS AMERICAN PROCTOLOGIC SOCIETY, 50th ANNIVERSARY. Hard. Pp. 217, with many illustrations. New York, N. Y., 1949, Yorke Publishing Company.

WORLD SURGERY—1950. By Stephen A. Zieman, M.A., M.D., F.A.C.S., F.I.C.S., Abstract and News Editor, Journal of International College of Surgeons. Hard. Price $6.00. Pp. 177, with 53 illustrations. Philadelphia, 1950, J. B. Lippincott Company.

PRACTICAL GYNECOLOGY. By Walter J. Reich, M.D., F.A.C.S., F.I.C.S., and Mitchell J. Nechtow, M.D., Cook County Hospital, Chicago, Ill. Hard. Price $10.00. Pp. 449, with 187 illustrations. Philadelphia, 1950, J. B. Lippincott Company.

BUCHANAN'S MANUAL OF ANATOMY. Edited by F. Wood Jones, D.Sc., M.Sc., M.B., B.S., F.R.S., F.R.C.S., F.R.A.C.S., Royal College of Surgeons, England. Hard. Price $8.50. Ed. 8. Pp. 1,616, with many illustrations. Baltimore, Md., 1950, Williams & Wilkins Company.

TISSUE CULTURE TECHNIQUE. By Gladys Cameron, Department of Biology, Washington Square College, New York University. Hard. Price $4.20. Ed. 2. Pp. 191, with some illustrations. New York, 1950, Academic Press Inc.

CRANIOPLASTY. By David L. Reeves, A.B., M.D., Consultant in Neurological Surgery, Santa Barbara Cottage Hospital, Santa Barbara, Calif. Hard. Price $3.00. Pp. 119, with many illustrations. Springfield, Ill., 1950, Charles C Thomas, Publisher.

TUMORS OF THE HEAD AND NECK. By Grant E. Ward, M.D., F.A.C.S., and James W. Henrick, M.D., M.S., Department of Surgery, School of Medicine, University of Maryland. Hard. Price $15.00. Pp. 832, with many illustrations. Baltimore, Md., Williams & Wilkins Company.

BONE & JOINT DISEASES. By Vernon Luck, M.D., M.S., F.A.C.S., F.I.C.S., Assistant Clinical Professor of Orthopedic Surgery, University of Southern California. Hard. Price $16.50. Pp. 614, with many illustrations. Springfield, Ill., Charles C Thomas, Publisher.

THE BREAST. Edited by F. D. Saner, M.B., B.Ch., F.R.C.S., Surgeon, Royal Northern Hospital. Hard. Price $8.50. Pp. 316, with many illustrations. Baltimore, Md., 1950, Williams & Wilkins Company.